

Emergency Use Instructions for Healthcare Providers: **Moderna COVID-19 Vaccine for Primary, Additional, and/or Booster Doses**

The Centers for Disease Control and Prevention (CDC) is issuing Emergency Use Instructions (EUI) to provide information about the use of the COVID-19 vaccine by Moderna (Spikevax), which is approved (licensed) by the Food and Drug Administration (FDA) for the prevention of COVID-19 in individuals ages 18 years and older.¹ The CDC-issued EUI provide information for the use of this vaccine that are beyond the FDA-approved labeling. The CDC-issued EUI provide information on the following uses of the COVID-19 vaccine by Moderna for:

- A longer interval of 4–8 weeks between the first and second primary dose of Moderna COVID-19 vaccine for persons ages 12 years and older, particularly for individuals at higher risk of mRNA COVID-19 vaccine-associated myocarditis.
- Delaying the second primary dose in persons ages 12 years and older who recently had SARS-CoV-2 infection, by 3 months from symptom onset or positive test (if infection was asymptomatic)
- Primary dose(s), including for those with certain immunocompromising conditions or those with incomplete primary series, for persons ages 12 years and older who received primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines².
- Booster dose(s), including for those with certain immunocompromising conditions, for persons ages 18 years and older who received primary or booster vaccination with certain non-FDA authorized or approved COVID-19 vaccines².
- An additional dose in persons ages 18 years and older with certain immunocompromising conditions who received primary vaccination with the Janssen (Johnson & Johnson) COVID-19 Vaccine.
- A 3-month interval for a first booster dose after an mRNA vaccine primary series for persons ages 18 years and older who are moderately or severely immunocompromised.
- A second booster dose in persons ages 18–49 years without certain immunocompromising conditions who received both a primary dose and first booster dose with the Janssen COVID-19 Vaccine. A second booster dose in persons ages 50 years and older is [authorized under EUA](#).
- Revaccination of moderately or severely immunocompromised persons ages 12 years and older who received certain therapies (indicated below) and received dose(s) of COVID-19 vaccine prior to or during treatment.
 - Received COVID-19 vaccine dose(s) during treatment with B-cell-depleting therapies over a limited period
 - Received COVID-19 vaccine dose(s) prior to or during treatment involving hematopoietic cell transplant (HCT) or chimeric antigen receptor (CAR)-T-cell therapy

mRNA vaccines are preferred for persons with moderate or severe immune compromise. The COVID-19 vaccine by Pfizer-BioNTech under EUI also allow similar uses as an alternative mRNA COVID-19 vaccine to Moderna, and the same or similar recommendations in the EUI also apply to the use of the COVID-19 vaccine by Pfizer-BioNTech under EUI. See the [Pfizer-BioNTech COVID-19 EUI Fact Sheet for Healthcare Providers](#).

Refer to CDC’s [Interim Clinical Considerations](#) for specific recommendations on use of the COVID-19 vaccine by Moderna allowed under the EUI. Relevant information is detailed in the sections titled: “People who received COVID-19 vaccine outside the United States”, “People who received COVID-19 vaccine as part of a clinical trial”, and “Recommendations for COVID-19 vaccination in moderately or severely immunocompromised

¹ Spikevax is the proprietary name for the product licensed under the Biologics License Application (BLA). The Moderna COVID-19 Vaccine has been available since December 18, 2020, pursuant to Emergency Use Authorization (EUA). The approved formulation of Spikevax and the FDA-authorized Moderna COVID-19 Vaccine for ≥ 12 years are the same formulation. Because of these features, and because Spikevax may be commonly referred to as the “Moderna COVID-19 Vaccine,” these EUI refer to this vaccine as the COVID-19 vaccine by Moderna.

² A non-FDA authorized or approved COVID-19 vaccine that is listed for emergency use by the World Health Organization, or is included in CDC’s [Technical Instructions for Implementing Presidential Proclamation Advancing Safe Resumption of Global Travel During the COVID-19 Pandemic](#) and [CDC’s Order](#), or that is a non-placebo part of a clinical trial within or outside the United States that is a WHO-EUL COVID-19 vaccine or a vaccine that is not listed for emergency use by WHO but for which a U.S. data and safety monitoring board or equivalent has independently confirmed efficacy in the United States (hereinafter “non-FDA authorized or approved COVID-19 vaccines”).

people.” For additional information about the COVID-19 vaccine by Moderna COVID-19, refer to the [Spikevax](#) package insert or the [Full Emergency Use Authorization \(EUA\) Prescribing Information](#) (FDA, 2022).

What are EUI and why is CDC issuing EUI for the COVID-19 vaccine by Moderna?

In 2013, the Pandemic and All-Hazards Preparedness Reauthorization Act included a new provision that allowed for the issuance of EUI to permit CDC to inform healthcare providers and recipients about certain uses of FDA-approved or cleared medical products. Specifically, EUI inform healthcare providers and recipients about such products’ approved, licensed, or cleared conditions of use. The CDC Director has statutory (legal) authority to create, issue, and disseminate EUI before or during an emergency.

The COVID-19 vaccine by Moderna was approved by the FDA on January 31, 2022 as a 2-dose primary series for active immunization to prevent COVID-19 in persons ages 18 years and older. CDC is issuing these EUI to provide information about use of the COVID-19 vaccine by Moderna for primary, additional, and/or booster doses that extend beyond its FDA-approved labeling as described further under “Who can receive the COVID-19 vaccine by Moderna” and “What are the doses and intervals of the COVID-19 vaccine by Moderna for primary, additional, and/or booster doses”.

What is COVID-19?

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that emerged in late 2019. It is predominantly a respiratory illness that can affect other organs. People with SARS-CoV-2 infection have reported a wide range of symptoms, ranging from no 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, and diarrhea.

Who can receive the COVID-19 vaccine by Moderna?

The below describes who can receive the COVID-19 vaccine by Moderna under EUI. The COVID-19 vaccine by Pfizer-BioNTech can also be used under EUI for similar uses as an alternative mRNA COVID-19 vaccine (see the [Pfizer-BioNTech EUI Fact Sheet for Healthcare Providers](#)).

- Persons ages 12 years and older, particularly those at higher risk of mRNA COVID-19 vaccine-associated myocarditis, may receive a second primary dose of the COVID-19 vaccine by Moderna after a longer interval of 4–8 weeks following the first primary dose.
- Persons ages 12 years and older who recently had SARS-CoV-2 infection may receive the second primary dose after a deferral period of 3 months from symptom onset or positive test (if infection was asymptomatic)
- Persons ages 12 years and older who received an incomplete primary series (e.g., only the first dose of 2-dose primary series) with certain non-FDA authorized or approved COVID-19 vaccines should receive a primary dose of the COVID-19 vaccine by Moderna.
- Persons ages 18 years and older who have received primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines should receive a booster dose of the COVID-19 vaccine by Moderna.
- Persons ages 18–49 years without certain immunocompromising conditions who received both a primary dose and a first booster dose of the Janssen COVID-19 Vaccine may receive a second booster dose of the COVID-19 vaccine by Moderna. A second booster dose in persons ages 50 years and older is [authorized under EUA](#).
- For certain moderately or severely immunocompromised persons:
 - Ages 12 years and older who received primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines should receive an additional primary dose of the COVID-19 vaccine by Moderna.
 - Ages 18 years and older who received primary vaccination with the Janssen COVID-19 Vaccine should receive an additional dose with the COVID-19 vaccine by Moderna.

- Ages 12 years and older who received certain therapies (indicated below) and received dose(s) of COVID-19 vaccine prior to or during treatment should be revaccinated with the COVID-19 vaccine by Moderna for any doses received before or during treatment.
 - Received COVID-19 vaccine dose(s) during treatment with B-cell-depleting therapies over a limited period
 - Received COVID-19 vaccine dose(s) prior to or during treatment involving HCT or CAR-T-cell therapy

What are the doses and intervals of the COVID-19 vaccine by Moderna for primary, additional, and/or booster doses?

- A second primary dose of the COVID-19 vaccine by Moderna (100 µg in 0.5 mL from red-capped multidose vial) should be administered intramuscularly to persons ages 12 years and older; this may be 4–8 weeks after the first primary dose. The approved interval is 4 weeks after the first dose, but an 8-week interval may be optimal for some people.
- A second primary dose of the COVID-19 vaccine by Moderna (100 µg in 0.5 mL from red-capped multidose vial) may be delayed by 3 months from symptom onset or positive test (if infection was asymptomatic) in persons ages 12 years and older who recently had SARS-CoV-2 infection
- A primary dose, including as an additional primary dose for those with certain immunocompromising conditions, of the COVID-19 vaccine by Moderna (100 µg in 0.5 mL from red-capped multidose vial) should be administered intramuscularly to persons ages 12 years and older at least 28 days after primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines.
- A first booster dose of the COVID-19 vaccine by Moderna (50 µg in 0.25 mL from red-capped multidose vial) should be administered intramuscularly for persons ages 18 years and older who completed an mRNA COVID-19 vaccine primary series or primary vaccination with a series that included certain non-FDA authorized or approved COVID-19 vaccines: at least 3 months after completion of primary vaccination for persons with certain immunocompromising conditions or at least 5 months after completion of primary vaccination for persons without certain immunocompromising conditions.
- A second booster dose with the COVID-19 vaccine by Moderna (50 µg in 0.25 mL from red-capped multidose vial) may be administered intramuscularly at least 4 months after the first booster dose to persons 18–49 years of age without certain immunocompromising conditions who received both a primary dose and first booster dose with the Janssen COVID-19 Vaccine.
- An additional dose with the COVID-19 vaccine by Moderna (100 µg in 0.5 mL from red-capped multidose vial) should be administered intramuscularly for persons ages 18 years and older with certain immunocompromising conditions at least 28 days after a primary dose with the Janssen COVID-19 Vaccine (e.g., 1 primary dose of the Janssen COVID-19 Vaccine followed by an additional dose with an mRNA COVID-19 vaccine at least 28 days after the primary dose). People who received both 1 primary dose and 1 booster dose of the Janssen COVID-19 Vaccine or 1 primary dose of the Janssen COVID-19 Vaccine followed by 1 booster dose of an mRNA COVID-19 vaccine should receive an additional dose with the COVID-19 vaccine by Moderna (100 µg in 0.5 mL from red-capped multidose vial) at least 2 months after the booster dose.
- Revaccination with the COVID-19 vaccine by Moderna for any doses received before or during treatment with certain therapies (indicated below) for persons ages 12 years and older.
 - Received COVID-19 vaccine dose(s) during treatment with B-cell-depleting therapies over a limited period: the suggested interval to start revaccination is about 6 months after completion of the B-cell-depleting therapy
 - Received COVID-19 vaccine dose(s) prior to or during treatment with HCT or CAR-T-cell therapy: revaccination at least 3 months after treatment

Refer to CDC’s [Interim Clinical Considerations](#) for specific and the latest dosing recommendations (e.g., number of doses, dosing intervals, revaccination) that may vary for individuals with certain medical conditions and/or in certain circumstances, which differ from or extend beyond the FDA-authorized and/or FDA-approved labeling.

See [Table 3](#) COVID-19 vaccination schedule for moderately or severely immunocompromised people in [CDC's Interim Clinical Considerations](#) for the latest dosing recommendations. On a case-by-case basis, providers of moderately or severely immunocompromised patients who are ages 12 years and older may administer the COVID-19 vaccine by Moderna outside of the FDA-authorized or FDA-approved labeling and CDC recommended dosing intervals based on clinical judgment when the benefits of vaccination are deemed to outweigh the potential and unknown risks for the recipient.

What are the formulations of the COVID-19 vaccine by Moderna that these EUI apply to?

The EUI apply to the FDA-approved formulation of the COVID-19 vaccine by Moderna (supplied in a red-capped multidose vial containing 5.5 or 7.5 mL of vaccine). The formulation supplied in a red-capped multidose vial is the same formulation that is FDA-authorized under EUA and FDA-licensed under BLA on January 31, 2022. This formulation provides primary doses (100 µg in 0.5 mL) and booster doses (50 µg in 0.25 mL). FDA has explained that the FDA-approved Spikevax and the EUA-authorized Moderna COVID-19 Vaccine supplied in red-capped multidose vials have the same formulation and can be used [interchangeably](#) without presenting any safety or effectiveness concerns.

What other presentations of the COVID-19 vaccine by Moderna are available?

On March 29, 2022, a dark blue-capped multidose vial containing 2.5 mL of vaccine was FDA-authorized for booster dose use only and provides booster doses (50 µg in 0.5 mL). This formulation can be used to administer booster dose(s) of COVID-19 vaccine by Moderna as recommended in the CDC's [Interim Clinical Considerations](#).

What are the common side effects with the COVID-19 vaccine by Moderna?

Adverse reactions following administration of the vaccine that have been reported in clinical trials and/or post authorization include injection site pain, fatigue, headache, muscle pain, joint pain, chills, nausea, vomiting, axillary swelling/tenderness, fever, injection site swelling, injection site redness, and rash.

What are possible serious side effects with the COVID-19 vaccine by Moderna?

Anaphylaxis and other severe allergic reactions, myocarditis, pericarditis, and syncope have been reported following administration of the vaccine outside of clinical trials. The observed risk of myocarditis and pericarditis is highest in males 18 through 24 years of age. Some observational analyses of postmarketing data suggest that there may be an increased risk of myocarditis and pericarditis in males under 40 years of age following the second dose of the COVID-19 vaccine by Moderna relative to other authorized or approved mRNA COVID-19 vaccines. Although postmarketing data following a booster dose of mRNA vaccines are limited, available evidence suggests a lower myocarditis risk following a booster dose relative to the risk following the primary series second dose.

Who should not receive the COVID-19 vaccine by Moderna?

Do not administer the COVID-19 vaccine by Moderna to persons with known history of a severe allergic reaction (e.g., anaphylaxis) to a previous dose or any component of the vaccine (see *Contraindications, and Warnings and Precautions* sections in the [Spikevax](#) package insert or [Full EUA Prescribing Information](#) as well as CDC's [Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States](#) for additional considerations).

What information should be provided to persons receiving a primary, additional, and/or booster dose of the COVID-19 vaccine by Moderna as described in the EUI?

- Provide the [EUI Fact Sheet for Recipients and Caregivers](#).
- Provide a CDC COVID-19 Vaccination Record Card to the recipient or their caregiver with the lot number and date of administration recorded for the primary, additional, or booster dose of the COVID-19 vaccine by Moderna.

- Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a 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. For more information, visit: www.cdc.gov/vsafe.

What is the available supporting evidence for use of the COVID-19 vaccine by Moderna for additional primary or booster doses in people who received a primary vaccination with non-FDA authorized or approved COVID-19 vaccines?

CDC has not systematically evaluated the safety, immunogenicity, and efficacy of an additional dose of the COVID-19 vaccine by Moderna (as either an additional primary dose for certain immunocompromised persons or as a booster dose) following receipt of primary vaccination with a non-FDA authorized or approved COVID-19 vaccine. However, studies of COVID-19 vaccine boosting in the United Kingdom have shown that a third dose of AstraZeneca, Moderna, or Pfizer-BioNTech COVID-19 vaccines successfully boosted immune responses in people who had been primed with two doses of Pfizer-BioNTech or AstraZeneca COVID-19 vaccines approximately 3 months earlier. Levels of binding (IgG) and neutralizing antibodies, including against Delta variant, were generally higher when an mRNA vaccine was used as either a heterologous or homologous boost (Munro et al., 2021)). Frequencies of local and systemic adverse reactions in the 7 days post booster vaccination were higher with heterologous than homologous boosters and in those aged under 70 years when compared to older recipients. Among all mRNA vaccines, the 100 microgram COVID-19 vaccine by Moderna was the most reactogenic (Munro et al., 2021).

WHO's Strategic Advisory Group of Experts (SAGE) on Immunization has noted that although data are currently limited on the safety, immunogenicity, and effectiveness of heterologous versus homologous additional doses, evolving evidence suggests that use of a heterologous vaccine for an additional dose may be more immunogenic than a homologous series. In its recommendations for an additional dose in certain immunocompromised people and in people aged 60 years and over who received Sinopharm BIBP or Sinovac-CoronaVac COVID-19 vaccines as a 2-dose primary series, WHO has advised that countries can consider heterologous additional doses based on supply availability (WHO SAGE, 2021a-c).

More than 80 countries are using boosters after non-FDA authorized or approved COVID-19 vaccines. Countries such as the United Kingdom (JCVI, 2021a-b), Canada (National Advisory Committee on Vaccination, 2021), Germany, and France have recommended heterologous dosing, including with use of the Moderna COVID-19 vaccine, for an additional primary series and/or booster dose based on their reviews of available immunological and safety data, as well as the epidemiology of COVID-19 and other contextual factors.

Effectiveness of a Moderna COVID-19 Vaccine (0.25 mL [50 µg of mRNA]) booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 vaccine (homologous or heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Moderna COVID-19 Vaccine (0.25 mL [50 µg of mRNA]) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series and from immunogenicity data from an independent Phase 1/2 open-label clinical trial ([NCT04889209](https://clinicaltrials.gov/ct2/show/study/NCT04889209)) conducted in the United States that evaluated a booster dose (0.5 mL [100 µg of mRNA]) of the Moderna COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks (range 12 to 20 weeks) prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to

administration of the booster dose and on Day 15 after the booster dose. A booster response to the Moderna COVID-19 Vaccine (0.5 mL [100 µg of mRNA]) was demonstrated regardless of primary vaccination.

Recent studies indicate that additional doses in people who are moderately or severely immunocompromised are safe and can increase antibody response. Small studies in solid organ transplant recipients in Toulouse, Strasbourg, and Baltimore demonstrate immunogenicity of a 4th mRNA dose when administered 1–2 months after the 3rd dose (Kamar et al., 2021; Benotmane et al., preprint; Alejo et al., 2021). Multiple studies, including COV-BOOST and the NIH mix-and-match study demonstrated safety and immunogenicity of a booster dose in the general population when administered at intervals as short as 3 months following a 2-dose primary series (Munro et al., 2021; Atmar et al., preprint). Finally, multiple countries have implemented booster doses at least 3 months after primary vaccination in the general population (e.g., UK, Germany, Netherlands).

What is the available supporting evidence for a longer/extended interval (8 weeks) between the first and second dose in the mRNA vaccine primary series schedule?

New evidence suggests that an interval longer than 4 weeks between primary series doses may reduce the risk of myocarditis and result in greater immunogenicity and effectiveness, such that there may be greater benefits and fewer risks with this dosing interval; however, the benefit of delaying the second dose beyond an interval of 8 weeks may be limited.

Several studies provide evidence that indicate greater immunogenicity and vaccine effectiveness (VE) following a longer interval between the first and second dose of the mRNA primary series.

- Neutralizing antibody titers were higher following an extended dosing (6–14 weeks) interval with mRNA vaccine, compared to a standard 3–4 week interval (Payne, 2021; Grunau 2021; Amirthalingam, 2021; Parry, 2022).
- Among an observational cohort of SARS-CoV-2 infection naïve health care workers (n=334) in the United Kingdom, persons who received Pfizer-BioNTech COVID-19 Vaccine following an extended dosing interval (6–14 week) had higher neutralizing antibody titers and antigen-specific B cell responses 4 weeks after their second dose, compared to persons with a short interval (3–4 week) (Payne, 2021).
 - Investigators observed sustained B and T cell responses, noting that the longer interval between vaccine doses may promote efficient T cell expansion and long-term memory cell persistence (Payne, 2021).
- In a large test-negative design study to evaluate VE among adults aged ≥18 years in British Columbia and Quebec, Canada, two-dose mRNA VE against infection and hospitalization was significantly higher with a longer dosing interval (7–8 weeks vs. 3–4 weeks) (Skowronski, 2021). VE appeared to plateau at the 7–8 week interval.
- A test-negative case control study among adults aged 50–89 years in England demonstrated that Pfizer-BioNTech VE was higher with longer (>6 weeks) intervals compared to short (3–4 weeks) intervals for all age groups (Amirthalingam, 2021).

A longer interval between the first and second dose of mRNA vaccines may improve safety, especially for young men.

- In an unpublished (preprint) retrospective population-based cohort using Canada’s provincial vaccine registry and passive vaccine safety surveillance between December 2020 and September 2021, reported rates of myocarditis/pericarditis among all persons were greater with shorter intervals (3–4 weeks) between dose 1 and dose 2 compared to extended intervals (≥8 weeks) for both Moderna (unadjusted rate ratio [RR]= 5.2, 95% CI 2.6–10.0) and Pfizer-BioNTech (RR=5.5, 95% CI 3.1–9.6) (Buchan, preprint).
- The lower reported rates of myocarditis/pericarditis among persons receiving their second vaccine dose at extended intervals (≥8 weeks) was observed across schedules of mRNA vaccine primary series (i.e., Pfizer-Pfizer, Moderna-Moderna, Pfizer-Moderna) (Buchan, preprint).

Countries such as Australia, Canada, Denmark, Finland, France, Germany, Norway, Taiwan, and the United Kingdom have recommended extended mRNA vaccine primary series dosing for all persons or specific sub-groups, based on their reviews of available immunological, safety, and effectiveness data, as well as the epidemiology of COVID-19, operational considerations, and other contextual factors.

What is the available supporting evidence for use of the COVID-19 vaccine by Moderna for a second booster dose in people who have received a primary dose and first booster dose with Janssen COVID-19 Vaccine?

Real-world VE data from the use of COVID-19 vaccines in the U.S. have suggested that the Janssen COVID-19 Vaccine may have lower VE against both infection and severe disease compared to mRNA vaccines (IVY Network, 2021). Additionally, evidence is accumulating from observational studies in the U.S. to suggest individuals who have received Janssen COVID-19 Vaccine as both the primary vaccination and booster may have lower protection. In a recent study from CDC VISION network, VE against laboratory-confirmed COVID-19-associated emergency department and urgent care (ED/UC) encounters within 7-120 days since booster dose was 54% after 2 Janssen doses, 79% after 1 Janssen/1 mRNA dose, and 83% after 3 mRNA doses. VE estimates for the same vaccine regimens against laboratory-confirmed COVID-19-associated hospitalizations within 7-120 days since booster dose were 67%, 78%, and 90%, respectively (Natarajan et al., 2022).

What is the available supporting evidence for delaying a second primary dose in people who recently had SARS-CoV-2 infection by 3 months from symptom onset or positive test (if infection was asymptomatic)?

SARS-CoV-2 infection induces a robust humoral and cellular immune response (CDC, 2021). Additionally, a longer interval of at least 3 or 6 months between infection and vaccination may improve immune response by allowing time for the response to mature and avoiding interference from the vaccine (Abu-Raddad L, 2021; Zhong, 2021). Multiple large-scale studies have observed decreased risk of subsequent infection with antigenically similar variants by 80-93% for months after infection (CDC, 2021). Delaying vaccination for 3 months after infection may therefore help to maximize protection with minimal risk to the individual. However, robustness and duration of protection is variable (National Collaborating Center for Methods and Tools, 2021). The circulating variant, as well as individual-level factors such as age and comorbidities, can impact level of protection. For example, overall risk of reinfection increased during the Omicron wave, and protection from infection or vaccination, was less robust than against previous variants (Pulliam et al., 2022). Additionally, some populations (e.g., older adults, immunocompromised) may have decreased levels of protection following infection, necessitating an interval that balances the benefits and risks of delaying vaccination after infection at a population level.

Vaccination continues to be recommended regardless of the option for delaying vaccination after infection. Numerous immunologic studies and a growing number of epidemiologic studies have shown that vaccinating previously infected individuals significantly enhances their immune response and effectively reduces the risk of subsequent infection, including in the setting of increased circulation of more infectious variants (CDC, 2021).

What is the available supporting evidence for revaccination of people who received COVID-19 vaccine during B-cell-depleting therapy administered over a limited period?

Studies of people on B-cell-depleting therapies indicate patients do not achieve adequate seroconversion or have a decreased odds ratio of seroconversion if they were vaccinated during therapy (Haggenberg, 2022a; Haggenberg, 2022b). The timing of vaccination relative to therapy influences vaccine immunogenicity; vaccination at least 6 months after therapy has demonstrated improved seroconversion (Kornek, 2022; Schietzel, 2022, Disanto, 2021). The option to be revaccinated for people who received vaccination during therapy would allow the opportunity to develop a more sufficient immune response.

Risk-Benefit of the COVID-19 vaccine by Moderna as Primary, Additional, and/or Booster Vaccination for Individuals Described in the EUI

The duration of vaccine-induced protection from primary vaccination with COVID-19 vaccines is unknown. Efficacy data from clinical studies of 2-dose primary series supported benefit of the COVID-19 vaccine by Moderna in preventing severe COVID-19 and supported its FDA approval. Effectiveness of an additional

primary dose of the COVID-19 vaccine by Moderna is inferred from immunogenicity data in immunocompromised adults who received a third 0.5 mL (100 µg of mRNA) primary dose. Rates of local or systemic adverse events with 50 µg booster dose were comparable to those observed after Dose 2 of the primary series (Miller, 2021; Das, 2021).

Effectiveness of a heterologous booster dose of COVID-19 vaccine by Moderna is inferred from data in adults who received a booster dose following primary vaccination with the Moderna COVID-19 vaccine or another FDA-authorized COVID-19 vaccine. Available data on the safety or efficacy of a Moderna COVID-19 vaccine dose after receipt of a non-FDA authorized or approved COVID-19 vaccine are limited. However, based on available information, it appears reasonable to anticipate that known and potential risks of an additional primary dose or a booster dose of the COVID-19 vaccine by Moderna may be outweighed by its likely benefit to enhance or restore protection by the primary vaccination, which might have waned over time, especially in people with immunocompromising conditions or taking immunosuppressive medications who may require a shorter interval for booster doses.

Refer to the CDC's [Interim Clinical Considerations for Use of COVID-19 Vaccines](#) for additional information.

Available Alternatives

Currently, the Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine are the only FDA-approved vaccines for which EUI provide for primary, additional, and/or booster dose administration.

Reporting Adverse Event or Medication Errors

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.

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.

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