

COVID-19 Vaccine, mRNA (Moderna)

80:12 • Vaccines (AHFS primary)

Special Alerts:

Emergency Use Authorization (EUA) Changes for COVID-19 Vaccine (Moderna): On March 29, 2022, the EUA for the Moderna COVID-19 vaccine was reissued to permit use of the vaccine as a second booster dose at least 4 months after receipt of a first booster dose of any FDA-authorized or approved COVID-19 vaccine product to individuals ≥ 50 years of age and certain immunocompromised individuals ≥ 18 years of age (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise). A booster only presentation of the Moderna COVID-19 vaccine is also available in multiple dose vials with dark blue caps and labels with a purple border. The booster dose only presentation of the Moderna COVID-19 vaccine is *not* authorized for use as the primary vaccination series. On June 17, 2022, the EUA for Spikevax[®] and the Moderna COVID-19 vaccine was reissued to permit use of the vaccine as a 2-dose primary vaccination series in individuals 12–17 years of age; an additional (third) primary series dose also was authorized for administration at least 1 month following the second dose of the COVID-19 vaccine (Moderna or Spikevax[®]) in certain immunocompromised individuals 12–17 years of age (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise). The Moderna COVID-19 vaccine also was authorized for use as a 2-dose primary vaccination series in individuals 6 months to 11 years of age; an additional (third) primary series dose also was authorized for administration at least 1 month following the second dose of the COVID-19 vaccine (Moderna) in certain immunocompromised individuals 6 months to 11 years of age (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise). For additional information, consult the EUA at <https://www.fda.gov/media/144636/download> and the fact sheets at <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/spikevax-and-moderna-covid-19-vaccine>

National Alert Network (NAN) Alert Regarding Influenza and COVID-19 Vaccine Mix-ups: On October 15, 2021, the National Alert Network (NAN) issued an alert to make vaccine providers aware of reports of accidental mix-ups between the influenza (flu) and COVID-19 vaccines. The alert is based on 16 cases reported to the Institute for Safe Medication Practices (ISMP) error reporting programs. Most of the reports ISMP has received involve administration of one of the COVID-19 vaccines instead of an influenza vaccine; in 3 cases, patients received an influenza vaccine instead of a COVID-19 vaccine. Because most of the errors were reported by consumers, details about the contributing factors were not provided in many cases. However, possible contributing factors include increased demand for vaccination services, the ability to administer the flu and COVID-19 vaccines during the same visit, syringes located next to each other, unlabeled syringes, distractions, and staffing shortages. The alert provides recommendations for preventing such vaccine mix-ups. For additional information, consult the NAN alert at <https://www.ismp.org/sites/default/files/attachments/2021-10/NAN-20211015.pdf>.

On January 31, 2022, COVID-19 Vaccine (Moderna) received full FDA approval for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals 18 years of age or older. An emergency use authorization (EUA) for the Moderna COVID-19 vaccine is still in effect and authorizes use of the vaccine as an additional (third) primary dose in certain immunocompromised individuals, and as a single homologous booster dose in individuals who have completed the primary series of this vaccine or as a single heterologous booster dose in individuals who have completed primary vaccination with another authorized or approved COVID-19 vaccine.

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■ COVID-19 vaccine (Moderna) is a nucleoside-modified mRNA vaccine used to stimulate active immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Uses

■ Prevention of Coronavirus Disease 2019 (COVID-19)

COVID-19 vaccine (Moderna) is an mRNA vaccine being investigated and used for the prevention of coronavirus disease 2019[†] (COVID-19) caused by SARS-CoV-2.

Although efficacy and safety of COVID-19 vaccine (Moderna) have not been definitely established, the vaccine is available under an FDA emergency use authorization (EUA) for active immunization to prevent COVID-19 in individuals ≥ 18 years of age. The EUA authorized use of the vaccine as a 2-dose primary vaccination series, an additional (third) primary dose in certain immunocompromised individuals, and as a single homologous booster dose in individuals who have completed the primary series of this vaccine or as a single heterologous booster dose in individuals who have completed primary vaccination with another authorized or approved COVID-19 vaccine.

The US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) has issued interim recommendations and clinical considerations for the use of COVID-19 vaccines, including dosage and administration, specific populations and situations, and cautionary information. There currently are 3 different COVID-19 vaccines available for use in the US, including 2 mRNA vaccines (Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine) and a viral-vectored vaccine (Janssen COVID-19 vaccine). COVID-19 vaccination is currently recommended for individuals ≥ 5 years of age in the US for prevention of COVID-19; however, the age groups approved or authorized to receive vaccination vary by vaccine product. In most situations, ACIP states that the mRNA vaccines are preferred over the Janssen COVID-19 vaccine for primary and booster vaccination because of the risks associated with the Janssen vaccine; however, the Janssen COVID-19 vaccine may be offered in certain situations. In patients eligible for an additional (third) primary mRNA COVID-19 vaccine dose (e.g., certain immunocompromised individuals), ACIP states that the same mRNA COVID-19 vaccine product should generally be used.

Emergency Use Authorization

On December 18, 2020, FDA issued the initial EUA for COVID-19 vaccine (Moderna) that permitted use of a 2-dose series of the vaccine to prevent COVID-19 in individuals ≥ 18 years of age. Since then, the EUA has been amended and reissued several times as the scope of authorization changed. The EUA for the Moderna COVID-19 vaccine now permits use as:

- A 2-dose (0.5 mL each) primary vaccination series in individuals 18 years of age or older.
- An additional (third) primary dose (0.5 mL) administered at least 1 month following the second dose of the COVID-19 vaccine (Moderna) in certain immunocompromised individuals 18 years of age or older (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise).
- A single homologous booster dose (0.25 mL) administered at least 5 months after completion of the primary series of the COVID-19 vaccine (Moderna) or a single heterologous booster dose (0.25 mL) after completion of a primary vaccination series with another authorized or approved COVID-19 vaccine in individuals 18 years of age or older. When a heterologous booster dose is used, the dosing interval is the same as that authorized for a booster dose of the vaccine product used for primary vaccination.

The EUA requires that the vaccine be administered by vaccination providers as authorized and that vaccination providers participate and comply with the terms and training required by CDC's COVID-19 vaccination program.

FDA issued the EUA for COVID-19 vaccine (Moderna) after concluding that emergency use of the vaccine for the prevention of COVID-19 met the criteria for issuance of an EUA for the following reasons: SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness; based on the totality of scientific evidence available to FDA, it is reasonable to believe that the Moderna COVID-19 vaccine may be effective in preventing COVID-19 and, when used under the conditions described in the authorization, the known and potential benefits outweigh the known and potential risks; and there are no adequate, approved, and available alternatives to the emergency use of the vaccine to prevent COVID-19.

The EUA requires that vaccination providers administering the Moderna COVID-19 vaccine comply with certain mandatory requirements. These requirements include providing the recipient or caregiver with information consistent with the EUA fact sheet and ensuring that all vaccination administration errors and all serious adverse events potentially attributable to the vaccine are reported as specified in the fact sheet.

For additional information, consult the Moderna COVID-19 vaccine EUA letter of authorization (<https://www.fda.gov/media/144636/download>), EUA fact sheet for healthcare providers (<https://www.fda.gov/media/144637/download>), and EUA fact sheet for recipients and caregivers (<https://www.fda.gov/media/144638/download>).

Clinical Experience

Primary Vaccination in Adults.

Efficacy and safety of COVID-19 vaccine (Moderna) for the prevention of COVID-19 are being evaluated in an ongoing multicenter, randomized, double-blind, placebo-controlled, phase 3 clinical trial in adults ≥ 18 years of age with no known history of SARS-CoV-2 infection (NCT04470427; mRNA-1273-P301; COVE study). At the time of FDA review for the EUA, the efficacy analysis population had been followed for a median of 9 weeks after the second dose and data indicated that the Moderna COVID-19 vaccine was 94.1% effective in preventing symptomatic, laboratory-confirmed COVID-19 occurring at least 14 days after the second dose of the 2-dose vaccination series compared with placebo. After issuance of the EUA, the study protocol was amended to include an open-label portion that will follow participants for up to 2 years.

The phase 3 COVE trial enrolled adults ≥ 18 years of age who were randomized 1:1 to receive 2 IM doses given 28 days apart of the Moderna COVID-19 vaccine (100 mcg for each dose) or normal saline placebo; randomization was stratified by age and risk criteria into 3 groups (18 to < 65 years of age without comorbidities [not at risk for progression to severe COVID-19], 18 to < 65 years of age with comorbidities [at risk for progression to severe COVID-19], ≥ 65 years of age with or without comorbidities). The study allowed for inclusion of participants with stable preexisting medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection; immunocompromised individuals and those with a known history of SARS-CoV-2 infection were excluded. The primary efficacy end point is efficacy of the vaccine in preventing laboratory-confirmed, symptomatic COVID-19 (as defined in the protocol) with onset at least 14 days after the second dose in participants with negative SARS-CoV-2 status at baseline. Among the 28,207 per-protocol participants included in the interim primary efficacy analysis for the EUA (14,134 in the vaccine group and 14,073 in the placebo group), there were 11 cases of symptomatic COVID-19 with onset at least 14 days after the second dose among vaccine recipients and 185 cases among placebo recipients, corresponding to a vaccine efficacy of 94.1%. Final analysis of efficacy and safety data from the blinded portion of the COVE trial included 28,451 per-protocol participants who were followed for a median of 212 days. In the final per-protocol analysis, there were 55 cases of symptomatic COVID-19 among vaccine recipients and 744 cases among placebo recipients, corresponding to a vaccine efficacy of 93.2% starting at least 14 days after the second dose of the primary vaccination series.

Additional primary efficacy analyses indicated that vaccine efficacy generally was consistent across subgroups defined by age, sex, race, ethnicity, and risk for severe disease. Vaccine efficacy in participants ≥ 65 years of age was 86.4% compared with 95.6% in younger adults. Analyses by time interval since completion of the primary vaccination series demonstrated that efficacy of vaccine remained $> 90\%$ through at least 4 months following the second dose of the primary vaccination series.

Secondary efficacy end points include prevention of severe COVID-19, asymptomatic COVID-19, death due to COVID-19, and COVID-19 occurring at least 14 days after the first dose. At the time of FDA's efficacy review for the EUA, there were a total of 30 cases of severe COVID-19 (as defined in the protocol) reported at least 14 days after the second dose (9 required hospitalization, 1 fatality) in the per-protocol participants and these severe cases all occurred in the placebo group, suggesting benefit of the vaccine in preventing severe COVID-19. Final analysis of data reported a vaccine efficacy in preventing severe disease of 98.2% in the per-protocol population (106 severe cases in the placebo group versus 2 in the vaccine group) starting 14 days after the second dose of the primary vaccination series. For prevention of asymptomatic COVID-19 infection, vaccine efficacy was 63% starting 14 days after the second dose of the primary vaccination series. COVID-19-related deaths occurred in 3 individuals in the placebo group and 1 in the COVID-19 vaccine (Moderna) group; however, the participant in the COVID-19 vaccine (Moderna) group had only received 1 dose of the vaccine.

Additional Primary Dose in Immunocompromised Adults.

Efficacy and safety of administration of a third primary dose of the Moderna COVID-19 vaccine were evaluated in a double-blind, randomized, placebo-controlled trial that included 120 solid organ transplant recipients (NCT04885907). Individuals included in the study were adults who had previously received various solid organ transplants (heart, kidney, kidney-pancreas, liver, lung, pancreas), had a functioning graft, had no history of COVID-19, and previously had received a 2-dose vaccination series of the Moderna COVID-19 vaccine administered at the recommended interval; exclusion criteria included treatment with immune globulin IV (IGIV) in the previous 4 weeks, treatment with rituximab in the previous 6 months, and treatment for acute rejection in the previous 30 days. Patients were randomized 1:1 to receive a third dose of the Moderna COVID-19 vaccine or saline placebo approximately 2 months after the second vaccine dose (60 transplant recipients in each group). At baseline (i.e., prior to the third vaccine dose), immunosuppressive therapy, the degree of immunosuppression, existing levels of anti-SARS-CoV-2 antibodies, and other patient characteristics were similar between both groups (median age was 66.6 years, median time from transplantation to the third vaccine dose was 3.16 years); immunosuppressive therapy included prednisone (77%), calcineurin inhibitors (98%),

mycophenolate (75%), azathioprine (10%), and sirolimus (9%). The primary outcome was the percentage of patients with anti-SARS-CoV-2 antibodies at 4 weeks indicating a significant immune response (defined as titer of antibody against the spike protein receptor-binding domain [RBD] of 100 units/mL or greater). Results indicated that anti-RBD antibody levels at 4 weeks after the third vaccine dose were 100 units/mL or greater in 55% of those who received a third dose of the Moderna COVID-19 vaccine compared with 17.5% of those who received placebo. The trial had short follow-up and lacked sufficient power to detect differences in clinical outcomes following the third vaccine dose in solid organ transplant recipients.

Booster Doses in Adults.

Efficacy and safety of the Moderna COVID-19 vaccine as a homologous booster dose after completion of the primary vaccination series are being evaluated in an ongoing open-label phase 2 clinical trial where participants ≥ 18 years of age received a single booster dose of the vaccine at least 6 months after receiving the second dose of the primary vaccination series. None of the participants had serologic or virologic evidence of a prior SARS-CoV-2 infection. The primary immunogenicity analysis population included 149 participants who were compared to a random subset of 1055 participants who received 2 doses of the Moderna COVID-19 vaccine in the phase 3 COVE study. The effectiveness of the booster dose (0.25 mL) was evaluated through neutralizing antibody titers (ID50) against a pseudovirus expressing the SARS-CoV-2 spike protein. The ID50 at 28 days after the booster dose was compared to the ID50 at 1 month after completion of the primary vaccination series in the random subset of participants from the COVE study. Analyses demonstrated that immunobridging criteria for a booster response were met for ID50 geometric mean titers (defined as a ≥ 4 -fold increase from baseline) but not for ID50 seroresponse rates.

Efficacy and safety of the Moderna COVID-19 vaccine as a heterologous booster dose after completion of the primary vaccination series with another authorized or approved COVID-19 vaccine are being evaluated in an ongoing phase 1/2 trial. At the time of FDA EUA review for booster doses, 458 participants 19–85 years of age who had no history of a prior SARS-CoV-2 infection were evaluated; participants had completed primary vaccination with a COVID-19 vaccine (Janssen, Moderna, or Pfizer-BioNTech) and were randomized 1:1:1 to Moderna COVID-19 vaccine (0.5 mL), Janssen COVID-19 vaccine, or Pfizer-BioNTech COVID-19 vaccine. A booster response to the Moderna COVID-19 vaccine based on neutralizing antibody titers against a pseudovirus expressing the SARS-CoV-2 spike protein was demonstrated regardless of primary vaccination.

Dosage and Administration

■ General

Pretreatment Screening

- Screen all individuals for contraindications and precautions prior to vaccination.

Patient Monitoring

- Monitor all individuals who receive a COVID-19 vaccine for immediate adverse reactions according to CDC (ACIP) guidelines. ACIP states that the following individuals should be observed for 30 minutes after receiving the vaccine: those with a history of immediate allergic reaction of any severity to a non-COVID-19 vaccine or injectable therapy; those with a contraindication to a different type of COVID-19 vaccine (i.e., viral vector); those with a history of a non-severe, immediate allergic reaction to a previous dose of COVID-19 vaccine; and those with a history of anaphylaxis due to any cause. All other individuals should be observed for 15 minutes. A longer period of observation may be indicated for some individuals based on clinical concern (e.g., vaccine recipient develops pruritus and swelling at the injection site during the observation period).
- Instruct vaccine recipients to seek immediate medical care if they develop signs or symptoms of an allergic reaction after the observation period is complete. (See Hypersensitivity Reactions under Cautions.)

Premedication and Prophylaxis

- Antipyretics or analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory agents) may be taken for the treatment of postvaccination local or systemic symptoms, if medically appropriate. However, routine premedication for the purpose of preventing postvaccination symptoms in individuals receiving a COVID-19 vaccine is *not* currently recommended because information regarding possible impact on antibody response to the vaccine is not available at this time.
- Premedication with antihistamines prior to vaccination to prevent allergic reactions is *not* recommended; antihistamines do not prevent anaphylaxis and may mask cutaneous symptoms, which could lead to a delay in the diagnosis and management of anaphylaxis. (See Hypersensitivity Reactions under Cautions.)

Dispensing and Administration Precautions

- Appropriate medications and supplies for managing immediate allergic reactions *must* be immediately available in the event that an acute anaphylactic reaction occurs following administration of COVID-19 vaccines. Healthcare personnel who are trained and qualified to recognize signs and symptoms of anaphylaxis and administer IM epinephrine should be available at vaccination sites at all times. Vaccination locations that anticipate vaccinating large numbers of people (e.g., mass vaccination clinics) should plan adequate staffing and

- supplies (including epinephrine) for assessment and management of anaphylaxis. (See Hypersensitivity Reactions under Cautions.)
- Syncope (vasovagal or vasodepressor reaction; fainting) may occur following administration of parenteral vaccines; such reactions usually occur within 15 minutes following vaccine administration and are reported most frequently in adolescents and young adults. Take appropriate measures to decrease the risk of injury if the vaccine recipient becomes weak or dizzy or loses consciousness (e.g., instruct the individual to sit or lie down during and for 15 minutes after vaccination). If syncope occurs, observe the vaccine recipient until symptoms resolve.

Other General Considerations

- At the time the first COVID-19 vaccine dose is administered, a vaccination record card that provides the date when the recipient needs to return for additional vaccine dose(s) should be given to the vaccine recipient or their caregiver; vaccine recipients should be counseled on the importance of completing the 2-dose primary vaccination series and receiving a booster dose to optimize protection against COVID-19.
- Provide vaccine recipients or their caregiver with information on CDC's v-safe program, a voluntary smartphone-based tool that uses text messaging and web surveys to monitor for adverse effects in individuals who have received a COVID-19 vaccine.
- Prior to vaccination, counsel vaccine recipients or their caregivers on local and systemic adverse effects that may occur following vaccination. Unless a contraindication to vaccination exists, ACIP recommends that vaccine recipients should be encouraged to complete the 2-dose vaccination series of the Moderna COVID-19 vaccine even if they experience local or systemic adverse effects following the first dose since this optimizes protection.
- Individuals who receive COVID-19 vaccines should follow current CDC guidance to protect themselves and others. This may include wearing a mask in certain settings with substantial or high levels of viral transmission; following application federal, state, local, tribal, or territorial laws, rules, and regulations; and following CDC travel guidance and any applicable local business or workplace guidance.

■ Administration

COVID-19 vaccine (Moderna) is administered *only* by IM injection into the deltoid. Confirm the dosing volume prior to administration (0.5 mL for a primary series dose or 0.25 mL for a booster dose).

IM Injection

COVID-19 vaccine (Moderna) is supplied as a frozen suspension in multiple-dose vials. The frozen vials *must* be shipped and stored (long-term) at a temperature between -50 to -15°C. For short-term storage, unopened multiple-dose vials of the vaccine may be stored in a refrigerator (2–8°C) for up to 30 days prior to first use. (See Stability.) Prior to use, the vials should be removed from the freezer and thawed either in a refrigerator (2–8°C) or at room temperature (15– 25°C). If thawed under refrigeration, allow the vials to stand at room temperature for 15 minutes before use.

The Moderna COVID-19 vaccine should not be diluted.

Thawed, unused vials (i.e., unpunctured) may be stored for up to 24 hours at 8–25°C. After the first dose of Moderna COVID-19 vaccine is withdrawn from the multiple-dose vial, the vial should be stored between 2–25°C and *must* be discarded if not used within 12 hours after first vial entry. The date and time of first use should be recorded on the vial label.

Vials of vaccine should be swirled gently after thawing and between withdrawal of each dose and should *not* be shaken.

For primary series doses, 0.5 mL of the vaccine should be withdrawn from the vial and for booster doses, 0.25 mL of the vaccine should be withdrawn from the vial using aseptic technique and an appropriate syringe and needle (preferably with a low dead-volume syringe and/or needle); the vaccine should be administered immediately following preparation.

Moderna COVID-19 vaccine is supplied in 2 different multiple-dose vial presentations (5.5 mL vial and 7.5 mL vial); doses used for the primary vaccination series and for booster doses may be extracted from either vial presentation. When extracting only doses for the primary vaccination series, a maximum of eleven 0.5-mL doses (range: 10–11 doses) can be withdrawn from the 5.5 mL vial and a maximum of fifteen 0.5-mL doses (range: 13–15 doses) can be withdrawn from the 7.5 mL vial depending on the syringes and needles used. When extracting only booster doses or a combination of primary series and booster doses from either vial, the maximum number of doses that may be extracted from either vial presentation should not exceed 20 doses; do not puncture the vial stopper more than 20 times.

Because the vaccine does not contain preservatives, it is critical that any vaccine remaining in the vial that does not constitute a full 0.5-mL or 0.25-mL dose should be discarded and should *not* be pooled with vaccine from other vials to obtain a dose. If the vial stopper has been punctured 20 times, discard the vial and any remaining vaccine.

Thawing.

Thawing in a refrigerator (2–8°C): Multiple-dose vials of frozen Moderna COVID-19 vaccine containing 5.5 mL or 7.5 mL should be thawed for 2.5 or 3 hours, respectively, in a refrigerator. Unopened vials of the vaccine may be stored in a refrigerator (2–8°C) for up to 30 days prior to first use.

Thawing at room temperature (15–25°C): Multiple-dose vials of frozen Moderna COVID-19 vaccine containing 5.5 mL or 7.5 mL may be allowed to sit at room temperature for 1 or 1.5 hours, respectively, to thaw. Unopened vials of the vaccine may be stored for up to 24 hours at 8–25°C.

Thawed COVID-19 vaccine (Moderna) should appear as a white to off-white suspension and may contain white or translucent product-related particles. The thawed vaccine should *not* be used if it is discolored or contains other particles.

Vaccine that has been thawed *must* not be refrozen.

■ Dosage

Each primary series dose of the Moderna COVID-19 vaccine is 0.5-mL, which contains 100 mcg of mRNA (see Description). Each booster dose is 0.25 mL, which contains 50 mcg of mRNA. A 2-dose regimen of the Moderna COVID-19 vaccine is considered a complete primary vaccination series. Individuals should generally not receive more than one complete primary vaccination series for active immunization against COVID-19.

Individuals are considered fully vaccinated against COVID-19 at least 2 weeks after receiving a 2-dose vaccination series of an mRNA vaccine (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine).

ACIP states that doses for the primary vaccination series and the additional primary dose, if indicated, should be completed with the same vaccine product.

ACIP states that in *exceptional* situations when the mRNA COVID-19 vaccine used for the first dose cannot be determined or is not available, any available mRNA COVID-19 vaccine may be administered to complete the mRNA COVID-19 vaccination series. If 2 doses of *different* mRNA COVID-19 vaccines are administered in such situations (or inadvertently), the primary series is considered complete.

Additionally, ACIP states that, in limited, *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the vaccination series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), a single dose of the Janssen COVID-19 vaccine administered at least 28 days after the first dose of mRNA COVID-19 vaccine may be considered. An individual who receives a dose of an mRNA COVID-19 vaccine followed by a single dose of the Janssen COVID-19 vaccine under such exceptional circumstances should be considered to have received complete single-dose vaccination with Janssen COVID-19 vaccine (not a mixed vaccination series).

For booster doses, ACIP states that use of an mRNA COVID-19 vaccine is preferred in individuals ≥18 years of age even for those who received the Janssen COVID-19 vaccine for their single-dose primary series. However, if an mRNA vaccine cannot be given, offering the Janssen COVID-19 vaccine as a booster is preferable to not providing any COVID-19 vaccine booster. In individuals 12–17 years of age, only the Pfizer BioNTech COVID-19 vaccine can be used for the booster dose.

Adult Dosage

Table 1. Moderna COVID-19 Vaccine Primary Series, Additional Primary Dose, and Booster Dose Recommendations			
	PRIMARY SERIES	ADDITIONAL PRIMARY DOSE	BOOSTER DOSE
Indicated population	All individuals ≥18 years of age	Immunocompromised individuals ≥18 years of age	All individuals ≥18 years of age
Dose	100 mcg	100 mcg	50 mcg
Injection volume	0.5 mL	0.5 mL	0.25 mL
Recommended doses and interval	2 doses, administered 28 days apart	1 dose, administered ≥28 days after completion of primary series	1 dose, administered ≥5 months after completion of primary series (including additional dose)

Primary Vaccination Series.

Each *primary series* dose of the Moderna COVID-19 vaccine is 0.5 mL. The FDA EUA that permits use of COVID-19 vaccine (Moderna) for the prevention of COVID-19† states that adults ≥18 years of age should receive two 0.5-mL doses of the vaccine administered 1 month (28 days) apart.

The FDA EUA permits administration of an additional primary dose of 0.5-mL of the Moderna COVID-19 vaccine at least 28 days after the second dose in adults who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise. (See Individuals with Altered Immunocompetence under Cautions.)

Booster Dose.

Each *booster dose* of the Moderna COVID-19 vaccine is 0.25 mL. The dose and volume are the same when given as a homologous (same as the primary vaccine series) or heterologous (different from the primary vaccine series) booster.

The FDA EUA permits administration of a single homologous booster dose of 0.25 mL of the Moderna COVID-19 vaccine at least 5 months after completion of the primary vaccination series in individuals ≥18 years of age.

The FDA EUA permits administration of a single heterologous booster dose of 0.25 mL of the Moderna COVID-19 vaccine at least 5 months following completion of primary vaccination with another authorized or approved COVID-19 vaccine. When a heterologous booster dose is used, the dosing interval should follow the interval recommended for the vaccine product used for the primary series. For example, those who received a single-dose primary series with the Janssen COVID-19 vaccine can receive an mRNA COVID-19 vaccine booster dose at least 2 months (8 weeks) after completing their Janssen COVID-19 primary series.

Cautions

■ Contraindications

- Known history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine. (See Description.)
ACIP considers the following to be contraindications to vaccination with *both* mRNA COVID-19 vaccines (Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine):
- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or severe allergic reaction to a component of the vaccine (e.g., polyethylene glycol [PEG]).
- Known (diagnosed) allergy to a component of the vaccine (e.g., PEG).

■ Warnings/Precautions

Sensitivity Reactions

Hypersensitivity Reactions.

At the time that FDA's safety and efficacy analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating COVID-19 vaccine (Moderna) was performed for the EUA, hypersensitivity reactions had been reported in 1.5% of vaccine recipients and 1.1% of placebo recipients, but there were no reports of anaphylactic or severe hypersensitivity reactions with close temporal relation to the vaccine. Hypersensitivity events reported in the vaccine group that were likely related to vaccination included injection site rash and injection site urticaria. The trial excluded participants with known or suspected history of allergic reaction to components of the Moderna COVID-19 vaccine, but did not exclude participants with other allergies.

Although immediate allergic reactions have not been reported to date in clinical trials evaluating the Moderna COVID-19 vaccine, severe allergic reactions, including anaphylaxis, have been reported rarely following administration of mRNA COVID-19 vaccines outside of clinical trials.

Following issuance of the FDA EUA for the Moderna COVID-19 vaccine, safety monitoring data identified 10 cases of anaphylaxis among 4,041,396 individuals in the US who received the first dose of the vaccine (2.5 cases per million vaccine doses administered); this included 9 cases in individuals with a documented history of allergies or allergic reactions to drugs, contrast media, or food (5 with a history of anaphylaxis). The median interval from receipt of the vaccine dose to onset of symptoms was 7.5 minutes (range: 1–45 minutes); 9 of the 10 individuals had onset within 15 minutes and one had onset after 30 minutes. All 10 individuals were treated with epinephrine. No fatalities from anaphylaxis were reported; 4 individuals were treated in an emergency department and the other 6 were hospitalized (including 5 in an intensive care unit).

From December 21, 2020 to January 10, 2021, safety monitoring data for individuals who received the first dose of the Moderna COVID-19 vaccine identified 43 cases of nonanaphylactic allergic reactions; 26 of these cases (60%) were classified as nonserious. Commonly reported symptoms included pruritus, rash, itchy sensations in the mouth and throat, sensations of throat closure, and respiratory symptoms. The median interval from receipt of the vaccine dose to onset of symptoms was 15 minutes (range: less than 1 minute to 24 hours); in 30 cases (73%), onset of symptoms occurred within 30 minutes.

Delayed-onset local reactions (e.g., erythema, induration, pruritus, tenderness) around the injection site area have been reported in some vaccine recipients, including some clinical trial participants, after the first dose of an mRNA COVID-19 vaccine, including the Moderna COVID-19 vaccine. These local reactions may begin from a few days through the second week after the first dose and may be quite large. In some reported cases, such delayed-onset local reactions after the first vaccine dose resolved in a median of 6 days (range: 2–11 days), and some individuals had similar (but less severe) local reactions after the second dose of the vaccine. ACIP states that a delayed-onset local reaction after the first dose of an mRNA COVID-19 vaccine is *not* a contraindication or precaution to administration of the second dose. Therefore, individuals with such injection site reactions after the first dose of an mRNA COVID-19 vaccine should receive the second dose of the same vaccine at the recommended interval, preferably in the opposite arm.

If a hypersensitivity reaction, including anaphylaxis, occurs following COVID-19 vaccination, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Because anaphylactic reactions have been reported rarely following administration of COVID-19 vaccines, ACIP has issued interim guidance with contraindications

and precautions for use of COVID-19 vaccines pending further investigation. For the purposes of this interim guidance, ACIP states that an immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms such as urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis occurring within 4 hours following administration. Vaccination providers should attempt to determine whether reactions reported following vaccination with an mRNA COVID-19 vaccine are consistent with allergic reactions that would contraindicate additional doses of the mRNA COVID-19 vaccine (see Hypersensitivity Reactions under Cautions) or are reactions commonly observed following vaccination, such as vasovagal reactions or postvaccination adverse effects, that are not considered contraindications to receiving the second dose of the 2-dose vaccination series.

History of severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components (e.g., PEG): ACIP considers this a **contraindication** to vaccination with the mRNA COVID-19 vaccines. ACIP states that consideration can be given to using the Janssen COVID-19 vaccine in such individuals provided certain measures are taken. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/ensuring-safety/monitoring/cisa/index.html>) when making such decisions.

Known (diagnosed) allergy to a component of the vaccine (e.g., PEG): ACIP considers this a **contraindication** to vaccination with the mRNA COVID-19 vaccines. ACIP states that consideration can be given to using an alternative COVID-19 vaccine (Janssen COVID-19 vaccine) in such individuals. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/ensuring-safety/monitoring/cisa/index.html>) when making such decisions.

History of any immediate allergic reaction to any other vaccine or injectable therapy (i.e., IM, IV, or subcutaneous vaccines or therapies): ACIP considers this a **precaution**, but not a contraindication, to COVID-19 vaccination. ACIP states that a history of allergic reaction to subcutaneous immunotherapy for allergies (i.e., allergy shots) is **not** a contraindication or precaution to COVID-19 vaccination.

History of immediate allergic reaction to a vaccine or injectable therapy that contains multiple components (one or more of which is a component of a COVID-19 vaccine), but it is not known which component elicited the reaction: ACIP considers this a **precaution**, but not a contraindication, to the COVID-19 vaccine.

History of allergic reactions (including severe allergic reactions) not related to COVID-19 vaccines, other vaccines, or injectable therapies: ACIP states that allergic reactions related to food, pets, insects, venom, or environmental allergies and allergic reactions to oral medications (including the oral equivalents of injectable medications) are **not** a contraindication or precaution to COVID-19 vaccination. Latex allergy is **not** a contraindication or precaution since vial stoppers of COVID-19 vaccines are not made with natural rubber latex. Allergies to eggs or gelatin are **not** a contraindication or precaution since COVID-19 vaccines do not contain eggs or gelatin. In addition, a family history of allergies is **not** a contraindication or precaution to COVID-19 vaccination.

History of delayed-onset local reactions (e.g., erythema, induration, pruritus) around the injection site area after the first dose of an mRNA COVID-19 vaccine: ACIP states that these local reactions are **not** a contraindication or precaution for administration of the second dose of the mRNA COVID-19 vaccine. Such individuals should receive the second dose using the same mRNA COVID-19 vaccine used for the first dose at the recommended interval, preferably in the opposite arm.

If a **precaution** for COVID-19 vaccination is identified, ACIP recommends that a risk assessment be performed to help decide whether the individual should be vaccinated. The risk assessment should consider the risk of exposure to SARS-CoV-2, risk of severe disease or death due to COVID-19 (e.g., because of age or underlying medical conditions), the unknown risk of anaphylaxis (including fatal anaphylaxis) following COVID-19 vaccination in individuals with a history of immediate allergic reactions to other vaccines or injectable therapies, and ability to be vaccinated in a setting where appropriate medical care is immediately available to treat anaphylaxis if it occurs.

ACIP states that the following individuals should be monitored for 30 minutes after vaccination: those with a history of an immediate allergic reaction of any severity to any other vaccine or injectable therapy, those with a contraindication to a different type of COVID-19 vaccine (i.e., viral vector), those with a history of a non-severe, immediate allergic reaction to a previous dose of COVID-19 vaccine, and those with a history of anaphylaxis due to any cause not considered a contraindication; all other individuals should be observed for 15 minutes. In addition, vaccine recipients should

be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site.

Appropriate medications and supplies to assess and manage immediate allergic reactions (e.g., sufficient quantities of epinephrine in prefilled syringes or autoinjectors) *must* be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine. Early recognition of the clinical signs and symptoms of anaphylaxis is important since such reactions require immediate treatment. Individuals with suspected anaphylaxis should be immediately treated with IM epinephrine.

ACIP interim guidance regarding management of anaphylaxis at COVID-19 vaccination sites is available at the CDC website at <https://www.cdc.gov/vaccines/covid-19/clinicalconsiderations/managing-anaphylaxis.html> and <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>. When confronted with a complex COVID-19 vaccine safety question that is not readily addressed by ACIP guidance, US healthcare personnel and health departments can request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html>).

Lymphadenopathy

Lymphadenopathy, lymphadenitis, lymph node pain, injection-site lymphadenopathy, axillary swelling/tenderness, and axillary mass have been reported in clinical trials evaluating COVID-19 vaccine (Moderna). At the time that FDA's safety and efficacy analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the vaccine was performed for the EUA, lymphadenopathy (axillary swelling and tenderness on the vaccination arm) was reported in 21.4% of vaccine recipients younger than 65 years of age and 12.4% of vaccine recipients 65 years of age or older compared with 7.5 and 5.8% of placebo recipients in those age groups, respectively, and was reported more frequently after the second dose than the first dose.

Cases of unilateral axillary adenopathy, including palpable axillary mass, have been identified through self-detection or incidentally on breast imaging in individuals who received an mRNA COVID-19 vaccine outside of clinical trials. In some reported cases, axillary adenopathy on the same side as the vaccination site was seen on breast ultrasound performed 5–13 days after receipt of an mRNA COVID-19 vaccine. Vaccine-induced hyperplastic axillary adenopathy should be considered in the differential diagnosis if unilateral axillary adenopathy is identified on breast imaging in individuals who recently received an mRNA COVID-19 vaccine. Some experts suggest that consideration should be given to scheduling routine screening mammography or ultrasound prior to the first dose of an mRNA COVID-19 vaccine or 4–6 weeks following the second dose of the vaccine, if possible, and if this would not unduly delay appropriate care.

Clinicians also should consider that increased axillary lymph node or deltoid uptake has been detected on positron emission tomography (PET) or other imaging performed in individuals who recently received an mRNA COVID-19 vaccine, and detailed history regarding COVID-19 vaccination (date of vaccination, arm used for vaccine injection) should be obtained to guide optimal follow-up and avoid unnecessary biopsies in individuals undergoing such imaging.

Myocarditis and Pericarditis

There have been rare reports of acute myocarditis or pericarditis in recipients of mRNA COVID-19 vaccines (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine) during post-authorization and post-marketing surveillance; the reports suggest an increased risk of myocarditis and pericarditis following vaccination, particularly within 7 days following the second dose. Symptom onset typically occurs within 2–7 days (range: 0–40 days) after receipt of a dose of an mRNA COVID-19 vaccine, and such cases have been reported more frequently after the second vaccine dose than the first dose. Available observational data have suggested an increased risk of myocarditis and pericarditis with the Moderna COVID-19 vaccine as compared to other authorized or approved COVID-19 vaccines. The risk of myocarditis with booster doses has been relatively lower than the primary series second dose based on limited evidence.

Data to date indicate that myocarditis and pericarditis following vaccination with an mRNA COVID-19 vaccine have predominantly occurred in males <40 years of age; the risk is highest among males 18–24 years of age. Although some individuals were hospitalized for short periods and some required intensive care support, available data from short-term follow-up suggest that the majority of these individuals responded to conservative treatment with rapid improvement or resolution of symptoms. Additional data are needed regarding the potential for long-term sequelae.

The possibility of myocarditis and pericarditis should be considered in the differential diagnosis for any individual, particularly males 12–29 years of age, who develop acute chest pain, shortness of breath, or palpitations after receipt of an mRNA COVID-19 vaccine. During initial evaluation of suspected cases, the vaccine recipient should be queried about prior COVID-19 vaccination and pertinent medical, travel, and social history; in addition, assessment of ECG, troponin levels, and inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate should be considered. Expert consultation should be considered regarding diagnosis, management, and follow-up.

Individuals receiving an mRNA COVID-19 vaccine, especially males 12–29 years of age, should be informed about the possibility of myocarditis or pericarditis after receiving the vaccine and the possibility of myocarditis or pericarditis occurring following SARS-CoV-2 infection and advised to seek medical care if symptoms of myocarditis or pericarditis occur after vaccination.

If myocarditis or pericarditis occurs following receipt of a COVID-19 vaccine, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Individuals who developed myocarditis or pericarditis after a dose of an mRNA COVID-19 vaccine: Because it is unclear whether such individuals are at increased risk of further adverse cardiac effects following a subsequent dose of the vaccine, experts recommend that subsequent vaccine doses should be deferred until additional safety data are available. ACIP states that there may be certain circumstances when administration of a subsequent dose can be considered, taking into account the individual's personal risk of severe COVID-19 (e.g., age, underlying conditions), level of COVID-19 in the community and personal risk of infection, availability of additional data on the risk of myocarditis or pericarditis in such situations, and availability of additional data on the long-term outcomes of myocarditis and pericarditis in individuals who have received an mRNA COVID-19 vaccine. Individuals with a history of myocarditis or pericarditis after a dose of an mRNA COVID-19 vaccine who choose to receive a subsequent dose should wait until their episode of myocarditis or pericarditis has completely resolved, including resolution of symptoms attributed to myocarditis or pericarditis with no evidence of ongoing heart inflammation or sequelae as determined by the individual's clinical team, which may include a cardiologist, and special testing to assess cardiac recovery.

Individuals with a history of myocarditis or pericarditis unrelated to mRNA COVID-19 vaccination (e.g., prior to COVID-19 vaccination): Data are limited regarding the safety and efficacy of COVID-19 vaccines in such individuals. ACIP states that such individuals may receive any FDA-approved or FDA-authorized COVID-19 vaccine after the episode of myocarditis or pericarditis unrelated to COVID-19 vaccination has completely resolved, including resolution of symptoms attributed to myocarditis or pericarditis with no evidence of ongoing heart inflammation or sequelae as determined by the individual's clinical team, which may include a cardiologist, and special testing to assess cardiac recovery.

Thrombocytopenia

During post-authorization surveillance, there have been very rare reports of thrombocytopenia, including immune thrombocytopenia (ITP), in recipients of mRNA COVID-19 vaccines (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine). As of February 4, 2021, more than 18 million doses of the Pfizer-BioNTech COVID-19 vaccine and more than 16 million doses of the Moderna COVID-19 vaccine had been administered in the US, and FDA had identified 15 cases of thrombocytopenia in recipients of the Pfizer-BioNTech COVID-19 vaccine and 13 cases in recipients of the Moderna COVID-19 vaccine (reporting rates of 0.8 per million doses for both mRNA vaccines). FDA stated that this number of post-vaccination cases of thrombocytopenia does not suggest a safety concern attributable to mRNA COVID-19 vaccines.

As of April 24, 2021, data from the Vaccine Safety Datalink (VSD) regarding reports of cerebral venous sinus thrombosis (CVST) in recipients of mRNA COVID-19 vaccines identified a total of 11 CVST cases (3 in recipients of the Pfizer-BioNTech vaccine and 8 in recipients of the Moderna vaccine). However, only 6 were considered to be potential incident cases of CVST since 5 of the cases were ruled out based on individual history (e.g., history of head injury, history of cavernous sinus syndrome); thrombocytopenia was not reported in any of these patients. At the time of this analysis, 6.3 million doses of mRNA COVID-19 vaccines had been administered at the healthcare organizations included in the VSD network, and there were no confirmed cases of CVST with thrombocytopenia in recipients of the Pfizer-BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine.

Concomitant Illness

A decision to administer or delay vaccination in an individual with a current or recent febrile illness depends on the severity of symptoms and etiology of the illness.

ACIP states that a moderate or severe acute illness is a precaution for administration of vaccines and states that a risk assessment should be performed with potential deferral of vaccination. Deferring vaccination until an individual has recovered avoids superimposing adverse effects of the vaccine on the underlying illness or mistakenly concluding that a manifestation of the underlying illness resulted from vaccination.

Individuals with Current SARS-CoV-2 Infection.

ACIP recommends that COVID-19 vaccination be deferred in individuals with known *current* SARS-CoV-2 infection until they have recovered from the acute illness (if symptomatic) and until criteria for discontinuance of isolation have been met. This recommendation applies to individuals who experience SARS-CoV-2 infection before receiving any doses of COVID-19 vaccine and those who experience SARS-CoV-2 infection after receiving the first dose of an mRNA COVID-19 vaccine but before receiving the second dose of the vaccine. While there is no recommended minimum interval between SARS-CoV-2 infection and COVID-19 vaccination, evidence to date

suggests that the risk of reinfection is low in the period after initial infection, but may increase with time due to waning immunity.

Individuals with Prior SARS-CoV-2 Infection.

Available data suggest that COVID-19 vaccines can be given safely to individuals with evidence of *prior* SARS-CoV-2 infection. ACIP states that COVID-19 vaccination should be offered to individuals regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection, including those with prolonged post-COVID-19 symptoms. Completion of a COVID-19 primary vaccination series in previously infected individuals decreases the risk of future SARS-CoV-2 infection.

Data are not available to date regarding the safety and efficacy of administering COVID-19 vaccines to individuals who have received passive antibody therapy with investigational SARS-CoV-2-specific monoclonal antibodies or investigational COVID-19 convalescent plasma as part of treatment of COVID-19. (See SARS-CoV-2 Antibody Therapies under Drug Interactions.)

Individuals with a History of Multisystem Inflammatory Syndrome.

Data are not available to date regarding the safety and efficacy of COVID-19 vaccines in adults or children with a history of multisystem inflammatory syndrome (MIS-A or MIS-C, respectively). The mechanisms of MIS-A and MIS-C are not well understood, but include a dysregulated immune response to SARS-CoV-2 infection. It is unclear whether those with a history of MIS-A or MIS-C are at risk for recurrence of the same dysregulated immune response following reinfection with SARS-CoV-2 or in response to COVID-19 vaccination. ACIP recommends weighing these theoretical concerns against the known risks of COVID-19 following reinfection and the benefits of protection following COVID-19 vaccination. Although children with MIS-C have high antibody titers to SARS-CoV-2, it is unclear whether this correlates with protection against reinfection and the duration of protective antibody levels in such children is not known.

ACIP states that individuals with a history of MIS-A or MIS-C may choose to be vaccinated. Although a conversation between the vaccine recipient, their guardian(s), and their clinical team or a specialist may assist with decisions regarding COVID-19 vaccination in such individuals, a conversation with a healthcare provider is not required before vaccination. When making decisions regarding COVID-19 vaccination in those with a history of MIS-C, the benefits of vaccination are thought to outweigh the risks (MIS-like illness or myocarditis) if the following criteria are met: achievement of clinical recovery (including return to normal cardiac function), 90 days have passed since the diagnosis of MIS-C, the individual resides in an area of high or substantial community transmission of SARS-CoV-2 (or otherwise have an increased risk for exposure and transmission), and the onset of MIS-C preceded any COVID-19 vaccination. Those with a history of MIS-C that do not meet the previous criteria and those with a history of MIS-A may consider vaccination based on achievement of clinical recovery, increased personal risk of severe COVID-19 (e.g., age, underlying conditions), and timing of immunomodulatory therapies.

If MIS-A or MIS-C associated with a confirmed SARS-CoV-2 infection develops after receipt of a COVID-19 vaccine, referral to a specialist in infectious diseases, rheumatology, or cardiology should be considered. US healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html>).

If MIS-A or MIS-C occurs following COVID-19 vaccination, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Individuals with Underlying Medical Conditions

ACIP states that individuals with altered immunocompetence or certain underlying medical conditions may receive any COVID-19 vaccine approved or authorized by FDA, unless they have a contraindication to the vaccine. Current FDA-approved or FDA-authorized COVID-19 vaccines are not live vaccines, so they may be safely administered to immunocompromised individuals.

US healthcare personnel and health departments can request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html>) if they have concerns about vaccinating individuals with certain underlying medical conditions.

Individuals with Altered Immunocompetence.

Individuals with altered immunocompetence, including those receiving immunosuppressive therapy, may have diminished immune responses to vaccines, including the Moderna COVID-19 vaccine.

Clinical trial data indicate that moderately or severely immunocompromised individuals (e.g., solid organ transplant recipients receiving immunosuppressive therapies, those with solid tumors or hematologic malignancies undergoing active treatment) may have reduced immune responses following a 2-dose vaccination series of an mRNA COVID-19 vaccine compared with those who are not immunocompromised.

Data from small studies have demonstrated that administration of an additional dose of mRNA COVID-19 vaccine after the initial 2-dose vaccination series may enhance immune responses to the vaccine in some immunocompromised individuals. Results of a study evaluating the safety and effectiveness of an additional (third) primary dose of an mRNA COVID-19 vaccine in solid organ transplant recipients

indicate that the third dose is only moderately effective in increasing potentially protective antibody titers in such individuals.

ACIP recommends that individuals who are moderately or severely immunocompromised should follow booster recommendations for the general population. For those who have completed an mRNA COVID-19 primary vaccination series and an additional primary dose, a single booster dose should be administered. Booster doses should be administered at least 5 months after completion of the third (additional) mRNA vaccine primary dose; those who have not previously received a third mRNA vaccine primary dose should be administered the additional primary dose of the vaccine first, as long as 28 days have passed since completion of the primary vaccination series, followed by the single booster dose (with COVID-19 Moderna vaccine, or COVID-19 Pfizer-BioNTech vaccine) at least 5 months after completion of the additional primary dose.

Individuals with altered immunocompetence, including those who receive a third (additional) primary dose or a booster dose of the Moderna COVID-19 vaccine, should be counseled about the unknown safety profile and effectiveness of COVID-19 vaccines in immunocompromised populations and the potential for reduced immune responses and the need to continue following all current CDC guidelines for fully vaccinated individuals (e.g., wearing a mask, staying 6 feet apart from those outside their household).

Individuals with Autoimmune Conditions.

ACIP states that individuals with autoimmune conditions may receive any COVID-19 vaccine approved or authorized by FDA, unless they have a contraindication to the vaccine. Individuals with autoimmune conditions were included in clinical trials evaluating mRNA COVID-19 vaccines and safety and efficacy of the vaccines in this population were similar to those in the general population.

Recommendations for individuals with altered immunocompetence apply to individuals with autoimmune conditions who are immunocompromised because of drug therapy (e.g., high-dose corticosteroids, biologic agents). (See Individuals with Altered Immunocompetence under Cautions.)

Individuals with Liver Disease.

The American Association for the Study of Liver Diseases (AASLD) has released a consensus statement regarding use of COVID-19 vaccines in individuals who have chronic liver disease or are liver transplant recipients. These experts state that vaccination against COVID-19 is strongly recommended because of the increased risk of morbidity and mortality in adults with chronic liver disease, especially those with cirrhosis. AASLD also recommends that those with chronic liver disease receiving treatment with prednisone, antimetabolites, or biologic therapies and those with hepatocellular carcinoma who receive an mRNA COVID-19 vaccine should receive a third (additional) primary dose of the vaccine administered at least 28 days after the 2-dose primary series.

The AASLD consensus statement should be consulted for additional guidance on use of COVID-19 vaccines in individuals with chronic liver disease.

Individuals with a History of Guillain-Barré Syndrome (GBS).

To date, GBS has not been reported in clinical trials evaluating mRNA COVID-19 vaccines.

If GBS occurs following COVID-19 vaccination, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Individuals with a History of Bell's Palsy.

Although a causal relationship has not been established, several cases of Bell's palsy have been reported in COVID-19 vaccine trials.

Data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the Moderna COVID-19 vaccine identified 3 cases Bell's palsy (facial paralysis) in the vaccine group (one was a serious adverse event) and one case of Bell's palsy in the placebo group. Onset of Bell's palsy was 22, 28, or 32 days after the vaccine dose and 17 days after the placebo dose. FDA stated that available data are insufficient to determine a causal relationship with the vaccine.

ACIP states that, in the absence of a causal relationship between COVID-19 vaccines and Bell's palsy, individuals with a history of Bell's palsy may receive COVID-19 vaccination, unless they have a contraindication to the vaccine.

If Bell's palsy occurs following COVID-19 vaccination, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Individuals with Increased Bleeding Risk.

Individuals who have bleeding disorders or are receiving anticoagulant therapy and/or their caregiver should be advised about the risk of hematoma from IM injections.

ACIP states that IM vaccines may be given to individuals who have bleeding disorders if a clinician familiar with the individual's bleeding risk determines that the preparation can be administered IM with reasonable safety. In these cases, a fine needle (23 gauge or smaller) should be used to administer the vaccine and firm pressure applied to the injection site (without rubbing) for at least 2 minutes. In individuals receiving therapy for hemophilia, IM vaccines can be scheduled for administration shortly after a dose of such therapy.

Individuals receiving anticoagulation therapy presumably have the same bleeding risk as patients with clotting factor disorders and should follow the same guidelines

for IM administration. If possible, IM vaccines could be scheduled prior to use of an anticoagulant so that the individual's risk of bleeding is not increased by the drug's therapeutic action.

History of Dermal Filler Use

Administration of an mRNA COVID-19 vaccine to individuals who have received injectable dermal fillers (e.g., hyaluronic acid dermal fillers) has infrequently resulted in swelling at or near the site of dermal filler injection (usually face or lips) starting within 1–2 days after vaccination. This effect has been reported when the vaccine was administered 2 weeks to 6 months or longer after the last dermal filler injection, and appears to be temporary and resolves with medical treatment, including corticosteroid therapy. A similar inflammatory reaction at the site of dermal filler injections (lips, cheeks, tear troughs) was reported in at least one unvaccinated individual who was diagnosed with COVID-19 approximately 2 weeks after their last dermal filler injection and has been reported after natural influenza-like illness. Although the mechanism of these reactions is not known, it may be due to an inflammatory reaction resulting from an interaction between the immune response after vaccination and the dermal filler.

ACIP states that individuals who have received injectable dermal fillers may receive COVID-19 vaccination, unless they have a contraindication to the vaccine. However, such individuals should be advised to contact their healthcare provider for evaluation if they develop swelling at or near the site of dermal filler injection following vaccination.

Individuals Vaccinated Outside the US

Some individuals in the US may have previously received vaccination against COVID-19 in another country using a vaccine that is not approved or authorized by FDA and/or is not listed for emergency use by the World Health Organization (WHO). ACIP provides guidance on COVID-19 vaccination in such individuals.

Limitations of Vaccine Effectiveness

COVID-19 vaccine (Moderna) may not protect all vaccine recipients against COVID-19. The risk of SARS-CoV-2 infection cannot be fully eliminated in fully vaccinated individuals while there is continued widespread community transmission of COVID-19.

The Moderna COVID-19 vaccine is administered in a primary vaccination series of 2 doses given 1 month (28 days) apart (see Dosage under Dosage and Administration). At the time of the EUA issuance, limited data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the Moderna COVID-19 vaccine indicated that estimated vaccine efficacy was 80.2% following the first dose compared with 94.1% following the second dose. Vaccine recipients should be counseled on the importance of completing the 2-dose primary vaccination series to optimize protection against COVID-19.

Use of COVID-19 vaccines for outbreak management or for postexposure prophylaxis to prevent SARS-CoV-2 infection in individuals with a specific known exposure to the virus is unlikely to be effective and is not currently recommended. ACIP states that, because the median incubation period of SARS-CoV-2 infection is 4–5 days, it is unlikely that a dose of COVID-19 vaccine would provide an adequate immune response within the incubation period for effective postexposure prophylaxis.

The FDA-approved or FDA-authorized COVID-19 vaccines are both efficacious and effective against symptomatic SARS-CoV-2 infection, including severe forms of disease. A substantial amount of data is available that has evaluated the effectiveness of COVID-19 vaccines in real world conditions. Multiple analyses have demonstrated effectiveness of a 2-dose mRNA COVID-19 vaccine series against symptomatic and asymptomatic infections, severe disease, hospitalization, and death. Real world studies that have evaluated the efficacy of COVID-19 vaccines specifically against Delta or during times of substantial Delta circulation have reported effectiveness against SARS-CoV-2 infection, symptomatic disease, and hospitalization. Breakthrough infections have been observed but at a much lower rate than infections in unvaccinated individuals; vaccine effectiveness against severe disease remains high, including against the Delta variant, and generally symptoms and duration of SARS-CoV-2 infections have been attenuated. Literature examining the effectiveness of COVID-19 vaccines against infection, symptomatic disease, and clinical outcomes can be accessed in the International Vaccine Access Center's VIEW-Hub resource library (<https://view-hub.org/resources>). Vaccine effectiveness against emerging variants will need to be continuously monitored and recommendations for continued prevention measures in fully vaccinated individuals will evolve.

The high vaccine efficacy against symptomatic COVID-19 and initial evidence for reduced levels of viral mRNA and culturable virus in vaccinated individuals also suggests that the transmission risk is substantially reduced after vaccination. In individuals who are vaccinated and are infected with the Delta variant, the period of infectiousness is reduced as compared to unvaccinated individuals. Vaccination against COVID-19 has substantially reduced the burden of disease in the US through prevention of serious disease in vaccinated individuals and interruption of chains of transmission.

Based on the unknown duration of vaccine-induced protection and the unknown extent of protection against emerging SARS-CoV-2 variants, individuals who receive COVID-19 vaccination and are considered fully vaccinated (see Dosage under Dosage

and Administration) and those who have received a third primary dose or a booster dose of the vaccine should be counseled to continue to follow current CDC interim guidance for fully vaccinated individuals to protect themselves and others. This may include wearing a mask in certain settings with substantial or high levels of viral transmission; following federal, state, local, tribal, or territorial laws, rules, and regulations; and following CDC travel guidance and any applicable local business or workplace guidance. These recommendations (available at the CDC website at <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html>) should be consulted for information on precautionary measures that fully vaccinated individuals should take in various social situations and/or following exposure to someone with suspected or confirmed COVID-19.

Data are limited to date regarding vaccine protection in some immunocompromised individuals, including those receiving immunosuppressive drugs (e.g., drugs such as mycophenolate and rituximab used to suppress rejection of transplanted organs or to treat rheumatologic conditions), and such individuals should discuss the need for personal protective measures after COVID-19 vaccination with their healthcare provider.

If COVID-19 breakthrough infection occurs in an individual who has received one or more doses of a COVID-19 vaccine, COVID-19 treatment guidelines, such as those from the National Institutes of Health (<https://www.covid19treatmentguidelines.nih.gov/>) or Infectious Diseases Society of America (<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>), should be consulted for treatment decisions, including use of SARS-CoV-2-specific monoclonal antibodies, convalescent plasma, antivirals, or corticosteroids. Breakthrough infections in fully vaccinated individuals that result in hospitalization or death should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Duration of Immunity

The duration of protection against SARS-CoV-2 infection following completion of the 2-dose vaccination series of COVID-19 vaccine (Moderna) has not been fully evaluated. The immunogenicity of COVID-19 vaccines has been demonstrated through 6 to 8 months after completion of the primary vaccine series. However, waning antibody levels and reduced neutralization of variants have been documented, which has contributed to current ACIP recommendations for single booster doses.

Improper Storage and Handling

Improper storage or handling of vaccines may reduce or destroy vaccine potency resulting in inadequate or no immune response in vaccinees. All vaccines should be inspected on delivery and monitored during storage to ensure that the recommended storage temperatures are maintained.

COVID-19 vaccine (Moderna) must be shipped, stored, and handled under specific conditions at all times, including maintaining cold chain conditions and chain of custody, according to specifications in the EUA fact sheet for healthcare providers and guidance from the manufacturer and CDC. Vaccine that has been mishandled or has not been stored at the recommended temperatures should not be administered. (See Stability.)

If there are concerns about mishandling or defective or damaged vaccine, the manufacturer should be contacted at 866-663-3762 for guidance.

EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting

Safety and efficacy of COVID-19 vaccine (Moderna) have not been established.

Some data are available regarding adverse effects associated with use of the Moderna COVID-19 vaccine. (See Common Adverse Effects under Cautions.) Additional adverse effects, some of which may be serious, may become apparent with more widespread use of the vaccine.

All vaccine recipients should be monitored for immediate adverse reactions according to CDC (ACIP) guidelines.

Vaccine recipients or their caregivers should be provided with information on, and encouraged to participate in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received a COVID-19 vaccine to identify potential adverse effects. Information on v-safe is available at <https://www.cdc.gov/vsafe>.

It is mandatory that vaccination providers report all vaccine administration errors (even if not associated with an adverse event) and serious adverse events (irrespective of attribution to vaccination) that occur following vaccination and also report all cases of multisystem inflammatory syndrome (MIS) and COVID-19 that result in hospitalization or death in vaccine recipients to VAERS. VAERS reports can be completed and submitted online at <https://vaers.hhs.gov/reportevent.html> or faxed to 877-721-0366; the words "Moderna COVID-19 Vaccine EUA" should be included in the description section of the report. Information on submitting a VAERS report can be obtained by calling 800-822-7967 or emailing info@vaers.org. To the extent feasible, a copy of the VAERS form should also be provided to the manufacturer (Moderna) at ModernaPV@modernatx.com (email), 866-599-1342 (fax), or 866-663-3762 (phone).

The FDA fact sheet for healthcare providers for the Moderna COVID-19 vaccine available at the FDA website and at <https://www.modernatx.com/covid19vaccine-eua> should be consulted for requirements and instructions regarding reporting of adverse reactions and vaccination errors.

Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals

ACIP states that results of SARS-CoV-2 viral tests (nucleic acid amplification or antigen tests) are not affected by prior COVID-19 vaccination.

To evaluate for evidence of prior infection in an individual with a history of COVID-19 vaccination (e.g., for public health surveillance or diagnosis of MIS-C or MIS-A), a test that specifically evaluates IgM/IgG to the nucleocapsid protein should be used.

Antibody testing is *not* currently recommended to assess the need for COVID-19 vaccination in unvaccinated individuals or to assess for immunity to COVID-19 following COVID-19 vaccination. Antibody tests currently authorized for use under EUAs have variable sensitivity and specificity, as well as positive and negative predictive values, and are not authorized for assessment of immune response in individuals who have received COVID-19 vaccination. In addition, the serologic correlates of protection against SARS-CoV-2 have not been established, and antibody testing does not evaluate the cellular immune response, which may also play a role in vaccine-mediated protection. If antibody testing is performed following COVID-19 vaccination, additional doses of the same or different COVID-19 vaccine beyond the recommended vaccination series should *not* be administered based on results of antibody testing. If antibody testing was done after the first dose of an mRNA COVID-19 vaccine, the vaccination series should be completed regardless of antibody test results.

Interpretation of Tuberculosis Tests in Vaccinated Individuals

ACIP states that COVID-19 vaccination should *not* be delayed in situations when an immune-based method of tuberculosis testing (i.e., intradermal tuberculin skin test [TST] or serum interferon gamma release assay [IGRA]) is required or indicated.

ACIP states that TST or IGRA testing can be administered without regard to timing of COVID-19 vaccination.

Specific Populations

Pregnancy.

Data are insufficient to date regarding use of COVID-19 vaccine (Moderna) in pregnant women to inform vaccine-associated risks during pregnancy.

In a developmental toxicity study in female rats, there was no evidence of vaccine-related adverse effects on female fertility, fetal development, or postnatal development when a vaccine formulation (same quantity of mRNA and other ingredients as that in a single human dose of the Moderna COVID-19 vaccine) was given IM on days 28 and 14 prior to mating and on gestation days 1 and 13.

Available data suggest that, while the absolute risk is low, pregnant and recently pregnant women with COVID-19 are at increased risk of severe illness, including illness resulting in hospitalization, admission to an intensive care unit, mechanical ventilation, extracorporeal membrane oxygenation (ECMO), or death compared with women who are not pregnant. Pregnant and recently pregnant women with comorbidities such as obesity and diabetes mellitus may be at even higher risk of severe COVID-19. Additionally, pregnant women with COVID-19 are at increased risk of preterm birth and may be at increased risk of adverse pregnancy complications and outcomes, such as preeclampsia, coagulopathy, and stillbirth.

Post-authorization surveillance safety data are accumulating regarding COVID-19 vaccination during pregnancy and clinical trials evaluating the safety and efficacy of COVID-19 vaccines in pregnant women are underway or planned. Early data from VAERS, v-safe active surveillance, and v-safe pregnancy registry have not identified any safety concerns in pregnant women who were vaccinated late in their pregnancy or in their infants; additional evidence has not found an increased risk for miscarriage following receipt of an mRNA vaccine before 20 weeks gestation. There is some evidence that pregnant women who receive an mRNA vaccine (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine) during pregnancy have immune responses comparable to those observed in individuals who are not pregnant and may develop anti-SARS-CoV-2 antibody titers greater than those observed in women diagnosed with SARS-CoV-2 infection during pregnancy.

The Moderna COVID-19 vaccine cannot cause SARS-CoV-2 infection in the pregnant woman or her fetus.

FDA states that pregnancy is not a contraindication to use of the Moderna COVID-19 vaccine, and pregnant women should discuss potential benefits and risks of vaccination with their healthcare providers.

ACIP states that vaccination against COVID-19 is recommended for pregnant women. These experts state that evidence regarding the safety and efficacy of COVID-19 vaccines available from both animal and human studies indicates that the benefits of vaccination against COVID-19 during pregnancy outweigh any known or potential risks. For purposes of decisions regarding administration of both the primary vaccination series and a booster dose, ACIP recommends that pregnant and recently pregnant women (up until at least 42 days following the end of pregnancy) should be considered in the same group as individuals with underlying medical conditions.

The American College of Obstetricians and Gynecologists (ACOG) recommends that pregnant women be vaccinated against COVID-19. When recommending COVID-19 vaccination to pregnant women, ACOG suggests that clinicians review the available data on risks and benefits of vaccination, including the risks of not getting vaccinated, in the context of the individual's current health status and risk of exposure (e.g., possibility for exposure at work or home) and the possibility for exposing high-risk household members. In addition, the individual's values and perceived risk of various outcomes should be taken into account and autonomous decision-making should be respected and supported.

ACIP and ACOG state that a conversation between the pregnant woman and her clinical team may assist with decisions regarding use of COVID-19 vaccines; however, such a conversation is not required and written permission is not needed prior to vaccination.

ACIP and ACOG recommend that women who become pregnant after receiving the first dose of an mRNA COVID-19 vaccination series should receive the second dose according to the usual schedule, unless contraindicated.

ACOG states that Rh₀(D) immune globulin should not be withheld when indicated in an individual who is planning to receive or recently received a COVID-19 vaccine. (See Immune Globulins and Antibody Therapies under Drug Interactions.)

Adverse effects similar to those reported in non-pregnant individuals can occur following COVID-19 vaccination in pregnant women. Pregnant women who experience fever following COVID-19 vaccination should be counseled to take acetaminophen; acetaminophen also may be offered as an option for pregnant women experiencing other postvaccination symptoms.

A pregnancy exposure registry to monitor pregnancy outcomes in women exposed to the Moderna COVID-19 vaccine during pregnancy has been established. Women who are vaccinated with the Moderna COVID-19 vaccine during pregnancy are encouraged to enroll in the registry by calling 866-663-3762.

Individuals who receive a COVID-19 vaccine during pregnancy and those who become pregnant within 30 days after receiving a COVID-19 vaccine should be encouraged to participate in CDC's v-safe program. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Females and Males of Reproductive Capacity.

Routine pregnancy testing is not recommended before receiving a COVID-19 vaccine.

ACIP states that vaccination against COVID-19 is recommended for women currently trying to get pregnant and those who might become pregnant in the future. Women trying to become pregnant do not need to avoid pregnancy after COVID-19 vaccination.

ACOG recommends vaccination for all eligible individuals, including those who may consider future pregnancy.

There is no evidence that any COVID-19 vaccines approved or authorized by FDA affect current or future fertility. FDA states that there is no scientific evidence to suggest that the Moderna COVID-19 vaccine could cause infertility in women. In addition, infertility is not known to occur as a result of natural COVID-19 disease, further demonstrating that immune responses to the virus, whether induced by infection or a vaccine, are not a cause of infertility.

Lactation.

Limited data are available to assess whether COVID-19 vaccines administered to a woman who is breast-feeding has any effects on the breast-fed infant or milk production.

FDA states that breast-feeding is not a contraindication to use of the Moderna COVID-19 vaccine, and women who are breast-feeding should discuss the benefits and risks of vaccination with their healthcare providers.

ACIP states that vaccination against COVID-19 is recommended for lactating women. FDA-authorized COVID-19 vaccines administered to breast-feeding women cannot cause SARS-CoV-2 infection in the women or their infants.

ACOG recommends that lactating women be vaccinated against COVID-19. ACOG also states that theoretical concerns regarding the safety of vaccinating lactating women do not outweigh the potential benefits of receiving the vaccine and there is no need to avoid initiating breast-feeding or to discontinue breast-feeding in those who receive a COVID-19 vaccine.

Although there is some evidence that antibodies that develop following vaccination with mRNA COVID-19 vaccines are present in breast milk, additional data are needed to determine if these antibodies convey protection against SARS-CoV-2 infection in breast-fed infants.

Pediatric Use.

Safety and efficacy of COVID-19 vaccine (Moderna) have not been assessed in individuals younger than 18 years of age.

The FDA EUA permits use of the Moderna COVID-19 vaccine *only* in individuals 18 years of age or older.

Geriatric Use.

Individuals ≥65 years of age have been included in clinical trials evaluating COVID-19 vaccine (Moderna), and data from such individuals contribute to the overall assessment of safety and efficacy of the vaccine.

At the time that FDA's safety and efficacy analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial was performed for the EUA, 24.8% of participants were ≥65 years of age and 4.6% were ≥75 years of age. Subgroup efficacy analysis based on age indicated that vaccine efficacy in participants ≥65 years of age was 86.4% compared with 95.6% in those 18 to <65 years of age. Overall, there were no notable differences in safety profiles between participants ≥65 years of age and younger adults.

■ Common Adverse Effects

Data regarding the safety of COVID-19 vaccine (Moderna) are available from several clinical trials, including the ongoing randomized, double-blind, placebo-controlled, phase 3 trial (NCT04470427; mRNA-1273-P301; COVE study). At the time that FDA's safety analysis of the phase 3 trial was performed for the EUA, a total of 30,351 study participants 18 years of age or older (15,185 in the vaccine group and 15,166 in the placebo group) had received at least one dose.

Local adverse effects following administration of the Moderna COVID-19 primary vaccination series in clinical trials: Injection site pain (92%), axillary swelling/tenderness (19.8%), swelling (14.7%), and erythema (10%).

Systemic adverse effects following administration of the Moderna COVID-19 primary vaccination series in clinical trials: Fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), and fever (15.5%).

Data indicate that solicited local and systemic adverse effects usually occurred within the first 1–2 days after a dose of the Moderna COVID-19 vaccine, had a median duration of 2–3 days, and were reported more frequently after the second dose of the 2-dose vaccination series. Use of antipyretic or pain medication within 7 days after receiving the first or second vaccine dose was reported in 23.3 or 57.3%, respectively, of those 18–64 years of age and in 17.9 or 41.9%, respectively, of those 65 years of age or older.

Solid organ transplant recipients: Adverse event profile following a third dose of the Moderna COVID-19 vaccine in adult transplant (heart, kidney, kidney-pancreas, liver, lung, pancreas) recipients was similar to that following the second dose; no grade 3 or 4 adverse events were reported.

Local adverse effects following administration of booster dose in clinical trials: Injection site pain (76.3–86%), axillary swelling/tenderness (5.3–24.8%), swelling (2.6–6.2%), and erythema (2.6–5.4%). Systemic adverse effects following administration of booster dose in clinical trials: Fatigue (47.4–62%), headache (42.1–58.9%), myalgia (47.4–49.6%), arthralgia (39.5–41.9%), chills (18.4–40.3%), nausea/vomiting (7.9–12.4%), and fever (5.4–7.0%).

At the time that FDA's safety analysis of the phase 3 trial evaluating a 2-dose regimen of the Moderna COVID-19 vaccine was performed for the EUA, serious adverse events had been reported in 1% of vaccine recipients and 1% of placebo recipients. FDA considered 3 of the serious adverse events reported in the vaccine group to be possibly related to the vaccine (i.e., intractable nausea and vomiting in an individual 1 day after vaccination; facial swelling with onset 1–2 days after vaccination in 2 individuals with a history of injection of facial cosmetic dermal fillers).

At the time that FDA's safety analysis of the phase 3 trial evaluating a 2-dose regimen of the Moderna COVID-19 vaccine was performed for the EUA, serious adverse events had been reported in 1% of vaccine recipients and 1% of placebo recipients. FDA considered 3 of the serious adverse events reported in the vaccine group to be possibly related to the vaccine (i.e., intractable nausea and vomiting in an individual 1 day after vaccination; facial swelling with onset 1–2 days after vaccination in 2 individuals with a history of injection of facial cosmetic dermal fillers). As of August 16, 2021, no serious adverse events considered causally related had been reported in an ongoing phase 2 trial evaluating the safety and immunogenicity of a booster dose of the Moderna COVID-19 vaccine.

Although immediate allergic reactions have not been reported to date in clinical trials evaluating the Moderna COVID-19 vaccine, severe allergic reactions (including anaphylaxis) and other hypersensitivity reactions (e.g., rash, pruritus, urticaria) have been reported rarely when the vaccine was administered outside of clinical trials. (See Hypersensitivity Reactions under Cautions.)

Drug Interactions

■ Antithrombotic Agents

ACIP does not recommend taking aspirin or an anticoagulant before vaccination with any currently FDA-approved or FDA-authorized COVID-19 vaccination, unless they are taking these drugs as part of their routine medications.

■ Antiviral Agents

Use of antiviral agents at any interval before or after COVID-19 vaccination is unlikely to impair development of vaccine-induced protective antibody responses.

■ Immune Globulins and Antibody Therapies

Individuals receiving immune globulin (e.g., immune globulin IV [IGIV], Rh₀(D) immune globulin) and antibody therapies *not* specific for SARS-CoV-2 may receive COVID-19 vaccination, either concurrently with or at any interval before or after the immune globulin or antibody therapy since such products are unlikely to substantially

impair immune responses to the COVID-19 vaccine. ACIP states that there is no recommended minimum interval between receipt of antibody therapies not specific for SARS-CoV-2 and COVID-19 vaccination.

SARS-CoV-2 Antibody Therapies

Limited data are available regarding the safety and efficacy of administering COVID-19 vaccines to individuals who have received passive antibody therapy with investigational SARS-CoV-2-specific monoclonal antibodies (e.g., bamlanivimab and etesevimab, casirivimab and imdevimab, sotrovimab) or investigational COVID-19 convalescent plasma. Based on the estimated half-life of SARS-CoV-2 antibody therapies as well as the anticipated period of protection, individuals who have received passive antibody products as part of post-exposure prophylaxis or treatment for COVID-19 should temporarily defer COVID-19 vaccination as a precautionary measure to avoid any potential inference of the antibody therapy with vaccine-induced responses; COVID-19 vaccination should be deferred for 30 days and 90 days in patients who receive passive antibody products for post-exposure prophylaxis and COVID-19 treatment, respectively. However, COVID-19 vaccination is not contraindicated in individuals who have received passive antibody therapy within the past 90 days, and COVID-19 vaccine doses received within 90 days after receipt of passive antibody therapy do not need to be repeated.

If an individual who received COVID-19 vaccination subsequently develops COVID-19, ACIP states that prior receipt of COVID-19 vaccine should not affect treatment decisions, including the use of SARS-CoV-2-specific monoclonal antibodies or COVID-19 convalescent plasma, or the timing of such treatment.

■ Immunosuppressive Agents

Individuals receiving immunosuppressive therapy (e.g., cancer chemotherapy, corticosteroids, radiation) may have diminished or suboptimal antibody responses to vaccines, including the Moderna COVID-19 vaccine.

Although data are not currently available to establish safety and efficacy in individuals receiving immunosuppressive therapy, ACIP states that such individuals may receive COVID-19 vaccination if they have no contraindications to the vaccine. (See Individuals with Altered Immunocompetence under Cautions.)

Data are insufficient to date to inform optimal timing of COVID-19 vaccination for individuals planning to receive immunosuppressive therapies. However, based on general best practices for vaccination of immunocompromised individuals, ACIP states that COVID-19 vaccination should ideally be completed at least 2 weeks before initiation or resumption of immunosuppressive therapies whenever possible. When it is not possible to administer a complete COVID-19 vaccination series in advance, individuals receiving immunosuppressive therapy can still receive COVID-19 vaccination. The level of immunocompromise and timing of vaccination with the primary series, additional primary dose, booster dose, and revaccination is best determined with the individual's clinical team.

Based on general best practices for vaccination, ACIP states that COVID-19 vaccines may be administered to individuals receiving corticosteroids given topically or by local injection (e.g., intra-articular, intrabursal, or tendon injections) without regard to the timing of corticosteroid administration.

ACIP recommends revaccination with a primary vaccine series at least 3 months (12 weeks) after undergoing hematopoietic cell transplant or CAR-T-cell therapy in individuals who previously received the COVID-19 vaccine. It is further recommended that an additional primary dose be given if the individual is revaccinated with an mRNA COVID-19 vaccine and continues to have moderate or severe immune compromise. The level of immunocompromise and timing of vaccination is best determined with the individual's clinical team; the additional primary dose should be administered at least 28 days after the second primary dose.

■ Vaccines

Data are not available to date to assess the safety and immunogenicity of concomitant administration of the Moderna COVID-19 vaccine with other vaccines.

Extensive experience with non-COVID-19 vaccines has demonstrated that immunogenicity and adverse event profiles are generally similar whether vaccines are administered concomitantly or alone. However, it is not known whether reactogenicity of COVID-19 vaccines is increased when administered concomitantly with other vaccines, including those known to be more reactogenic (e.g., adjuvanted vaccines). Decisions to administer a COVID-19 vaccine concomitantly with other vaccine(s) should be based on whether routine immunizations with the other vaccines have been delayed or missed, the individual's risk of vaccine-preventable disease (e.g., during an outbreak or occupational exposures), and the reactogenicity profiles of the vaccines.

ACIP states that COVID-19 vaccines may be administered without regard to timing of other vaccines, including simultaneous administration on the same day. If a COVID-19 vaccine is administered concomitantly with other vaccines, each parenteral vaccine should be given at a different injection site and, if possible, the injection sites should be separated by at least 1 inch. ACIP states that, although the deltoid muscle can be used for more than one IM injection in adolescents and adults, COVID-19 vaccines and vaccines that are likely to cause a local reaction should be administered in different limbs, if possible.

Description

COVID-19 vaccine (Moderna) is a nucleoside-modified mRNA vaccine formulated in lipid nanoparticles (LNPs).

The mRNA contained in the Moderna COVID-19 vaccine encodes a full-length spike (S) glycoprotein of SARS-CoV-2 stabilized in a prefusion conformation with 2 proline substitutions (S-2P). Following IM injection, the LNPs in the vaccine enable delivery of the mRNA into host cells where it is released and translated to the encoded S antigen of SARS-CoV-2. The S antigen elicits an immune response to provide protection against SARS-CoV-2.

Data from a phase 1 clinical trial in healthy adults ≥ 18 years of age indicate dose-dependent antibody responses to a 2-dose regimen of the Moderna COVID-19 vaccine, with antibody responses boosted after the second dose. The Moderna COVID-19 vaccine induces both binding and neutralizing antibodies at levels comparable to or higher than those reported in convalescent serum obtained from individuals who have recovered from COVID-19; antibody responses in adults ≥ 56 years of age are similar to those reported in adults 18–55 years of age. The vaccine also directly activates T-cells, which eliminate infected cells and support B-cell responses; the T-cell response is predominantly type 1 helper (Th1).

COVID-19 vaccine (Moderna) available for use under the FDA EUA is provided as a frozen suspension in multiple-dose vials. Following thawing as directed by the manufacturer, each 0.5-mL dose of COVID-19 vaccine (Moderna) contains 100 mcg of mRNA encoding the S glycoprotein of SARS-CoV-2. Each dose of the vaccine also contains 4 different lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose. Each 0.25 mL dose of COVID-19 vaccine (Moderna) contains half of these ingredients.

The Moderna COVID-19 vaccine does not contain preservatives; vial stoppers are not made with natural rubber latex.

Advice to Patients

- Prior to administration of COVID-19 vaccine (Moderna), provide the vaccine recipient or their caregiver with information consistent with the Fact Sheet for Recipients and Caregivers: Emergency Use Authorization (EUA) of the Moderna COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 18 Years of Age or Older and given a copy of the fact sheet or directed to the manufacturer's website at <https://www.modernatx.com/covid19vaccine-eua> to obtain the fact sheet.
- At the time that the first dose of the Moderna COVID-19 vaccine is administered, inform the vaccine recipient or their caregiver that the vaccine is administered in a series of 2 doses given 1 month (28 days) apart and advise them of the importance of receiving the second dose of the 2-dose vaccination series to optimize protection against COVID-19. Give the vaccine recipient or their caregiver a vaccination card that provides the date when the recipient needs to return for the second vaccine dose and inform them of the importance of bringing the card when they return for the second dose.
- Inform individuals who are immunocompromised that they should receive a third dose of the Moderna COVID-19 vaccine at least 1 month (28 days) after the second dose. Advise such individuals that the third dose may still not provide full immunity to COVID-19 and that they should continue to follow preventative measures (e.g., wearing a mask, physically distancing).
- Provide the vaccine recipient or their caregiver with information on, and encourage participation in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received a COVID-19 vaccine to identify potential adverse effects; live telephone follow-up is provided if a medically important health impact is reported. Information on v-safe is available at <https://www.cdc.gov/vsafe>.
- Inform vaccine recipients or their caregivers that FDA authorized the emergency use of the Moderna COVID-19 vaccine, which is an investigational vaccine that has not received FDA approval, for use in individuals ≥ 18 years of age. Advise them that clinical trials have shown that a 2-dose series of the vaccine can prevent COVID-19; however, the duration of protection following vaccination is unknown and the vaccine may not protect everyone who receives it.
- Provide vaccine recipients or their caregivers with information on available alternative vaccines and the risks and benefits of those alternatives.
- Inform vaccine recipients or their caregivers about the significant known and potential risks and benefits of the Moderna COVID-19 vaccine, and the extent to which such risks and benefits are unknown. Inform them that local adverse effects (injection site pain, swelling, redness; tenderness and swelling of lymph nodes in the injected arm) and systemic adverse effects (fatigue, headache, muscle pain, joint pain, chills, nausea and vomiting, fever) have been reported in recipients of the Moderna COVID-19 vaccine.
- Inform vaccine recipients or their caregivers that myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported rarely in some recipients of the Moderna COVID-19 vaccine with symptom onset usually within a few days after the second vaccine dose. Importance of immediately seeking medical attention if chest pain, shortness of breath, or fast-beating, fluttering, or pounding heart occurs.

- Importance of vaccine recipient informing the vaccination provider of any allergies or fever. Advise vaccine recipients or their caregivers that there is a remote chance that the vaccine could cause a severe allergic reaction and such reactions would usually occur within a few minutes to 1 hour after receiving a dose of the vaccine and may include difficulty breathing, swelling of the face and throat, fast heartbeat, bad rash all over the body, and dizziness and weakness.
- Importance of vaccine recipient informing the vaccination provider if they have had a severe allergic reaction to any ingredient in the vaccine (e.g., PEG) or if they had a severe allergic reaction after receiving the first dose of the 2-dose vaccination series; importance of such individuals *not* receiving the vaccine.
- Importance of vaccine recipient informing vaccination provider if they previously received any other COVID-19 vaccine, have any medical conditions (e.g., bleeding disorders, myocarditis or pericarditis, immunocompromising diseases), or are receiving anticoagulants or immunosuppressive therapy.
- Importance of women informing clinicians if they are or plan to become pregnant or plan to breast-feed.

Overview® (see Users Guide). It is essential that the Emergency Use Authorization (EUA) prescribing information contained in the Fact Sheet for Healthcare Providers that is available at the FDA website and at <https://www.modernatx.com/covid19vaccine-eua> be consulted for more detailed information on dosage and administration, cautions, precautions, and contraindications, and for complete information on the conditions for use of the vaccine for the prevention of coronavirus disease 2019 (COVID-19) under the EUA, including mandated record keeping and reporting requirements.

Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

COVID-19 vaccine (Moderna) is not commercially available. FDA issued an emergency use authorization (EUA) for the Moderna COVID-19 vaccine that permits use of the vaccine as a 2-dose primary vaccination series in adults 18 years of age or older†, as a third primary dose† in certain immunocompromised adults, and as a single booster dose† after completion of the primary vaccination series with the same vaccine or another FDA-approved or FDA-authorized COVID-19 vaccine as specified in the EUA. Allocation of the vaccine for use under the EUA is being directed by the US government. The vaccine will be supplied directly from the manufacturer or authorized US distributor(s) and distributed to emergency response stakeholders as directed by the US government, including the CDC and/or other designee.

COVID-19 Vaccine, mRNA (Moderna)

Parenteral

Suspension, for IM use

100 mcg (of mRNA) per 0.5-mL dose

Moderna COVID-19 Vaccine,
ModernaTX

† Use is not currently included in the labeling approved by the US Food and Drug Administration.

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