

# COVID-19 Vaccine, mRNA

## (Moderna) (Systemic)

Nucleoside-modified mRNA vaccine used to stimulate active immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**Class:** 80:12 • Vaccines (AHFS primary)

**Brands\*:**

\*also available generically

### Special Alerts:

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>.

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## Uses

### Prevention of Coronavirus Disease 2019 (COVID-19)

- Being investigated and used for prevention of COVID-19† caused by SARS-CoV-2.
- Although efficacy and safety not definitely established, COVID-19 vaccine (Moderna) is available under an FDA emergency use authorization (EUA) for active immunization to prevent COVID-19 in individuals ≥18 years of age.
- On December 18, 2020, FDA issued the initial EUA that permitted use of the Moderna COVID-19 vaccine in individuals ≥18 years of age. On August 12, 2021, FDA reissued the EUA to authorize administration of a third dose of the vaccine in individuals ≥18 years of age who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise.
- The EUA requires that the vaccine be administered by vaccination providers as described in the EUA (see Dosage under Dosage and Administration) and that vaccination providers participate and comply with terms and training required by CDC's COVID-19 vaccination program, including monitoring and complying with CDC and/or emergency response stakeholder vaccine management requirements concerning obtaining, tracking, and handling the vaccine and reporting vaccine administration data to CDC and state/local jurisdiction's Immunization Information System (IIS) or other designated systems.

- FDA issued the EUA for the Moderna COVID-19 vaccine after concluding that emergency use of the vaccine for 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 vaccine may be effective in preventing COVID-19; and, when used under the conditions described in the authorization, known and potential benefits outweigh known and potential risks.
- The EUA for the Moderna COVID-19 vaccine authorizes that distribution of the vaccine will be controlled by the US government for use consistent with the terms and conditions of the EUA. (See Restricted Distribution under Preparations.)
- To mitigate risks of the vaccine, the EUA includes certain mandatory requirements (e.g., providing the recipient or caregiver with information consistent with the EUA fact sheet for recipients and caregivers, ensuring that all vaccination administration errors and all serious adverse events potentially attributable to the vaccine are reported as specified in the EUA fact sheet for healthcare providers). (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)
- 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>) for additional information.
- CDC's Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for use of the Moderna COVID-19 vaccine for prevention of COVID-19 in individuals ≥18 years of age.
- 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). ACIP does not state a preference for any specific COVID-19 vaccine approved or authorized by FDA when the vaccines are used within the scope of their respective biologics license application (BLA) or EUA and states that individuals should be encouraged to receive the earliest vaccine available to them. However, the Moderna COVID-19 vaccine is *not* interchangeable with other COVID-19 vaccines, including the Pfizer-BioNTech COVID-19 vaccine and the Janssen COVID-19 vaccine. (See Dosage under Dosage and Administration.)

## Dosage and Administration

### General

- *Must* have appropriate medications and supplies immediately available to assess and manage immediate allergic reactions in the event that an acute anaphylactic reaction occurs following administration of COVID-19 vaccines, including COVID-19 vaccine (Moderna). Healthcare personnel trained and qualified to recognize signs and symptoms of anaphylaxis and administer IM epinephrine should be available at vaccination locations 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.)
- Prior to administration of each dose of the Moderna COVID-19 vaccine, screen all individuals for contraindications and precautions to vaccination. Do not give the vaccine to those with a contraindication. (See Contraindications and see Warnings/Precautions under Cautions.)
- *Monitor all vaccine recipients for immediate adverse reactions according to CDC (ACIP) guidelines.* When administered to individuals with no contraindications to vaccination with an mRNA COVID-19 vaccine, ACIP states observe those who have a history of an immediate allergic reaction of any severity to any other vaccine or injectable therapy and those who have a history of anaphylaxis due to any cause not considered a contraindication for 30 minutes, and observe all other individuals for 15 minutes. A longer period of observation may be indicated in some individuals based on clinical concern (e.g., pruritus and swelling confined to the injection site develops during observation period). Instruct vaccine recipients 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. (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 risk of injury if a patient becomes weak or dizzy or loses consciousness (e.g., vaccinees should sit or lie down during and for 15 minutes after vaccination). If syncope occurs, observe patient until symptoms resolve.
- The Moderna COVID-19 vaccine is administered in a primary series of 2 doses given 1 month (28 days apart). (See Dosage under Dosage and Administration.) At the time that the first dose is administered, give vaccine recipient or their caregiver a vaccination record card that provides the date when the recipient needs to return for additional vaccine dose(s); counsel about the importance of completing the 2-dose primary vaccination series to optimize protection against COVID-19.
- Provide vaccine recipient or their caregiver with information on, and encourage participation in, CDC's v-safe program, a voluntary smartphone-based tool that uses text messaging and web surveys to monitor for adverse effects in COVID-19 vaccine recipients. (See

EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

- Prior to vaccination, counsel vaccine recipient or their caregiver about local and systemic adverse effects that may occur following vaccination. (See Cautions and see Advice to Patients.) Unless a contraindication to vaccination exists, ACIP recommends encouraging vaccinees to complete the 2-dose vaccination series even if they develop local or systemic adverse effects following the first dose since this optimizes protection.
- Antipyretics or analgesics (e.g., acetaminophen, NSAIDs) may be taken to treat postvaccination local or systemic symptoms, if medically appropriate. However, routine premedication for the purpose of preventing postvaccination symptoms in vaccinees is not currently recommended since information not available regarding possible impact on antibody response to COVID-19 vaccines. 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 delay diagnosis and management of anaphylaxis. (See Hypersensitivity Reactions under Cautions.)
- Counsel individuals who receive the Moderna COVID-19 vaccine and are considered partially or fully vaccinated against COVID-19 (see Dosage under Dosage and Administration) and those who have received a third primary dose to follow current CDC guidance to protect themselves and others. For fully vaccinated individuals, this may include wearing a mask in certain settings with substantial or high levels of viral transmission; following applicable federal, state, local, tribal, or territorial laws, rules, and regulations; and following CDC travel guidance and any applicable local business or workplace guidance. (See Limitations of Vaccine Effectiveness under Cautions.)

## Administration

### IM Administration

Administer *only* by IM injection into the deltoid.

The Moderna COVID-19 vaccine is supplied as a frozen suspension in multiple-dose vials that *must* be shipped and stored (long-term) at a temperature between -50 to -15°C. For short-term storage, may store unopened multiple-dose vials of the vaccine in a refrigerator (2–8°C) for up to 30 days prior to first use. (See Storage under Stability.)

Prior to use, remove the appropriate number of vials of the frozen Moderna COVID-19 vaccine from the freezer and thaw either in a refrigerator (2–8°C) or at room temperature (15–25°C). If thawed under refrigeration, allow vials to stand at room temperature for 15 minutes before use. (See Thawing under Dosage and Administration.)

*Do not dilute the Moderna COVID-19 vaccine.*

Swirl vials of vaccine gently after thawing and between withdrawal of each dose; do *not* shake.

To administer a dose, withdraw 0.5 mL of thawed Moderna COVID-19 vaccine from the vial using aseptic technique and an appropriate syringe and needle and administer immediately.

Moderna COVID-19 vaccine is supplied in 2 different multiple-dose vial presentations. There are multiple-dose vials containing a maximum of eleven 0.5-mL doses (range: 10–11 doses) and multiple-dose vials containing a maximum of fifteen 0.5-mL doses (range: 13–15 doses). Depending on type of syringes and needles used to withdraw doses from the multiple-dose vials, it may not be possible to extract more than 10 or more than 13 doses, respectively, from these vials. Each dose *must* contain 0.5 mL of the vaccine.

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 dose should be discarded and *not* be pooled with vaccine from other vials to create a dose.

Although data not available regarding safety and immunogenicity of concomitant administration with other vaccines, ACIP states that COVID-19 vaccines may be administered without regard to timing of other vaccines. (See Vaccines under Interactions.)

### Thawing

Thawing in a refrigerator (2–8°C): Thaw multiple-dose vials containing 11 or 15 doses for 2.5 or 3 hours, respectively, in a refrigerator. May store unopened vials in the refrigerator for up to 30 days prior to first use.

Thawing at room temperature (15–25°C): Allow multiple-dose vials containing 11 or 15 doses to sit at room temperature for 1 or 1.5 hours, respectively, to thaw. May store unopened vials for up to 24 hours at 8–25°C.

Thawed Moderna COVID-19 vaccine should appear as a white to off-white suspension and may contain white or translucent product-related particles; do *not* use if it is discolored or contains other particles.

Thawed vaccine *must* not be refrozen.

## Dosage

Administer the Moderna COVID-19 vaccine in a primary vaccination series of two 0.5-mL doses given 1 month (28 days) apart in adults ≥18 years of age†. Immunocompromised adults (i.e., solid organ transplant recipients or those diagnosed with conditions considered to have an equivalent level of immunocompromise) may receive a third 0.5-mL primary dose† of the Moderna COVID-19 vaccine administered ≥28 days after the second dose.

Each 0.5-mL dose contains 100 mcg of mRNA.

A 2-dose regimen of the Moderna COVID-19 vaccine is considered a complete primary vaccination series. Individuals should not receive more than one complete vaccination series for active immunization against COVID-19 (i.e., 2-dose regimen of an mRNA vaccine [Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine] or single dose of Janssen COVID-19 vaccine).

Individuals are considered fully vaccinated against COVID-19 ≥2 weeks after receiving the second dose of a 2-dose vaccination series of an mRNA vaccine (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19) or ≥2 weeks after receiving a single dose of the Janssen COVID-19 vaccine. For public health purposes, ACIP states that administration of a third (additional) primary dose of an mRNA COVID-19 vaccine in individuals with moderate to severe immunocompromise is *not* required to be considered fully vaccinated. Those who have a contraindication to vaccination or who otherwise cannot complete a vaccination series are not considered fully vaccinated.

Ensure that individuals who receive the first dose of the Moderna COVID-19 vaccine receive a second dose of the same vaccine at the recommended interval to complete the primary vaccination series.

FDA EUA that permits use of the Moderna COVID-19 vaccine specifies an interval of 1 month (28 days) between first and second vaccine doses. ACIP states schedule individuals to receive the second vaccine dose as close to the recommended day as possible, but not earlier than 1 month after the first dose; however, individuals who receive a second dose of the vaccine administered up to 4 days before or at any time after the recommended date can be considered fully vaccinated.

The Moderna COVID-19 vaccine is *not* interchangeable with the Pfizer-BioNTech COVID-19 vaccine or any other COVID-19 vaccine.

Safety and efficacy of a mixed vaccination series of mRNA COVID-19 vaccines not evaluated; individuals who receive a dose of the Moderna COVID-19 vaccine should complete the series using the same vaccine. Make every effort to determine which mRNA COVID-19 vaccine was used for first dose to ensure completion of the vaccination series using the same vaccine. ACIP states that in *exceptional* situations when the mRNA COVID-19 vaccine used for first dose cannot be determined or is no longer available, may administer any available mRNA COVID-19 vaccine approved or authorized by FDA using a minimum interval of 28 days between doses to complete the mRNA COVID-19 vaccination series. In situations where the same mRNA vaccine is temporarily unavailable, ACIP states it is preferable to delay the second dose to allow completion of the vaccination series using the same mRNA COVID-19 vaccine rather than administering a mixed vaccination series composed of 2 different mRNA COVID-19 vaccines. If 2 doses of *different* mRNA COVID-19 vaccines are administered for the primary series in such situations (or inadvertently), ACIP states such individuals are considered fully vaccinated against COVID-19 ≥2 weeks after receiving the second dose of mRNA vaccine.

Safety and efficacy regarding use of the viral-vectored vaccine (Janssen COVID-19 vaccine) after a dose of an mRNA COVID-19 vaccine *not* established. However, 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), may consider giving a single dose of the Janssen COVID-19 vaccine at least 28 days after the dose of mRNA COVID-19 vaccine. (See Hypersensitivity Reactions under Cautions.) In such exceptional circumstances, consider the individual to have received complete single-dose vaccination with Janssen COVID-19 vaccine, not a mixed vaccination series.

Report all vaccine administration errors and deviations from currently recommended dosage and vaccination schedule to the vaccinee and the Vaccine Adverse Event Reporting System (VAERS). (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.) Information on preventing and reporting COVID-19 vaccine administration errors and recommendations for specific actions to take if an administration error or deviation from recommended vaccination schedule occurs are available at CDC website at <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>.

## Adults

### Primary Vaccination Series

**IM:** FDA EUA that permits use for prevention of COVID-19† (see Prevention of Coronavirus Disease 2019 [COVID-19] under Uses) states that adults ≥18 years of age should receive two 0.5-mL doses of the vaccine administered 1 month (28 days) apart.

### >Third Primary Dose in Immunocompromised Adults

**IM:** FDA EUA permits administration of a third 0.5-mL primary dose at least 28 days after the second dose in solid organ transplant recipients or those diagnosed with conditions considered to have an equivalent level of immunocompromise. (See Individuals with Altered Immunocompetence under Cautions.)

## Cautions

### Contraindications

- Known history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine. (See Actions.)

ACIP considers the following to be contraindications to vaccination with *both* mRNA 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]).
- Immediate allergic reaction of any severity after a previous dose of an mRNA COVID-19 vaccine or known (diagnosed) allergy to a component of the vaccine (e.g., PEG).

## Warnings/Precautions

### Sensitivity Reactions

#### Hypersensitivity Reactions

Hypersensitivity reactions reported in 1.5% of vaccine recipients and 1.1% of placebo recipients in the ongoing phase 3 trial evaluating the Moderna COVID-19 vaccine; hypersensitivity events reported in the vaccine group and likely related to vaccination included injection site rash and injection site urticaria.

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

Following issuance of the FDA EUA for the **Pfizer-BioNTech COVID-19 vaccine**, safety monitoring data identified 21 cases of anaphylaxis among 1,893,360 individuals in the US who received the first dose of the vaccine (11.1 cases per million vaccine doses administered); this included 17 cases in individuals with documented history of allergies or allergic reactions to drugs or medical products, foods, or insect stings (7 of these had a history of anaphylaxis, including one after receipt of a dose of rabies vaccine and another after receipt of influenza vaccine). Median interval from receipt of vaccine to onset of anaphylaxis symptoms was 13 minutes (range: 2–150 minutes); 71% had onset of symptoms within 15 minutes after the dose and 90% were treated with epinephrine. No fatalities from anaphylaxis were reported; 17 individuals were treated in an emergency department and the other 4 were hospitalized (including 3 in an intensive care unit).

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 documented history of allergies or allergic reactions to drugs, contrast media, or food (5 of these had a history of anaphylaxis). Median interval from receipt of vaccine to onset of anaphylaxis 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 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 identified 43 cases of nonanaphylactic allergic reactions in individuals who received the first dose of the Moderna COVID-19 vaccine; 26 of these (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 vaccine to onset of symptoms was 15 minutes (range: <1 minute to 24 hours); 73% had symptom onset within 30 minutes.

Delayed-onset local reactions (e.g., erythema, induration, pruritus, tenderness) around the injection site area reported in some vaccine recipients, including some clinical trial participants, after 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 reaction after 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 vaccine dose. ACIP states that 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 vaccine 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, report the case to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Because anaphylactic reactions reported rarely following administration of COVID-19 vaccines, ACIP issued interim guidance with contraindications and precautions for use of COVID-19 vaccines pending further investigation. For 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. If reactions occur following vaccination with an mRNA COVID-19 vaccine, the vaccination provider should attempt to determine whether the reactions 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 (e.g., vasovagal reactions, postvaccination adverse effects) not considered contraindications to 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 both the Moderna and the Pfizer-BioNTech COVID-19 vaccines. ACIP states may consider 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), consider consultation with an allergist-immunologist to help determine if the individual can safely receive the Janssen COVID-19 vaccine. 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>) when making such decisions. Although safety and efficacy of administering the Janssen COVID-19 vaccine after an mRNA COVID-19 vaccine not established, ACIP states that, in those *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), may consider giving a single dose of the Janssen COVID-19 vaccine at a minimum interval of 28 days after the mRNA COVID-19 vaccine dose. (See Dosage under Dosage and Administration.)

**History of immediate allergic reaction of any severity to a previous dose of an mRNA COVID-19 vaccine or known (diagnosed) allergy to a component of the vaccine (e.g., PEG):** ACIP considers this a **contraindication** to vaccination with both the Moderna and the Pfizer-BioNTech COVID-19 vaccines. ACIP states may consider 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), consider consultation with an allergist-immunologist to help determine if the individual can safely receive the Janssen COVID-19 vaccine. 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>) when making such decisions. Although safety and efficacy of administering the Janssen COVID-19 vaccine after an mRNA COVID-19 vaccine not established, ACIP states that, in those *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), may consider giving a single dose of the Janssen COVID-19 vaccine at a minimum interval of 28 days after the mRNA COVID-19 vaccine dose. (See Dosage under Dosage and Administration.)

**History of polysorbate allergy:** ACIP considers this a **precaution** to vaccination with both the Moderna COVID-19 vaccine and the Pfizer-BioNTech COVID-19 vaccine. ACIP states polysorbate allergy is a contraindication to vaccination with the Janssen COVID-19 vaccine; may consider using an mRNA COVID-19 vaccine (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine) in such individuals. However, polysorbates are structurally related to PEG and there is potential for cross-reactive hypersensitivity. Consider consultation with an allergist-immunologist to help determine if the individual with polysorbate allergy can safely receive an mRNA COVID-19 vaccine. 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>) when making such decisions. If a decision is made to administer an mRNA COVID-19 vaccine to an individual with a contraindication to the Janssen COVID-19 vaccine (e.g., polysorbate allergy), administer the vaccine *only* in an appropriate setting under supervision of a healthcare provider experienced in management of severe allergic reactions.

**History of any immediate allergic reaction to any other vaccine or injectable therapy (i.e., IM, IV, or sub-Q vaccines or therapies):** ACIP considers this a **precaution**, but not a contraindication, to COVID-19 vaccination. ACIP states that history of allergic reaction to sub-Q 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 food, pet, insect, 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 first dose of an mRNA COVID-19 vaccine:** ACIP states that these local reactions are **not** a contraindication or precaution for administration of second dose of mRNA COVID-19 vaccine. Such individuals should receive second dose using the same mRNA COVID-19 vaccine used for first dose at the recommended interval, preferably in the opposite arm.

If a **precaution** for COVID-19 vaccination is identified, ACIP recommends performing a risk assessment to help decide whether the individual should be vaccinated. The risk assessment should consider risk of exposure to SARS-CoV-2 (e.g., because of residence in a congregate setting such as a long-term care facility, occupation), risk of severe disease or death due to COVID-19 (e.g., because of age or underlying medical conditions), 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.

When a COVID-19 vaccine, including the Moderna COVID-19 vaccine, is administered to individuals without a contraindication to such vaccines, ACIP states observe those with a history of an immediate allergic reaction of any severity to any other vaccine or injectable therapy and those with a history of anaphylaxis due to any cause not considered a contraindication for 30 minutes after the vaccine dose and observe all other individuals for 15 minutes. Instruct vaccine recipients 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 clinical signs and symptoms of anaphylaxis is important since such reactions require immediate treatment. Immediately treat individuals with suspected anaphylaxis with IM epinephrine.

ACIP interim guidance regarding early recognition of clinical signs and symptoms of anaphylaxis and guidance regarding preparation for and management of anaphylaxis at COVID-19 vaccination sites, including recommendations for medications and supplies to have immediately available and specific recommendations regarding therapeutic management of anaphylaxis, are 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 concerning an individual patient that is not readily addressed by ACIP guidance, US healthcare personnel or 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 reported in clinical trials evaluating COVID-19 vaccine (Moderna). Data from the ongoing phase 3 trial evaluating the Moderna COVID-19 vaccine identified lymphadenopathy (axillary swelling and tenderness on the vaccination arm) in 21.4% of vaccine recipients <65 years of age and 12.4% of vaccine recipients ≥65 years of age compared with 7.5 and 5.8% of placebo recipients in those age groups, respectively. Reported more frequently after second dose than first dose.

Unilateral axillary adenopathy, including palpable axillary mass, 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 same side as the vaccination site was seen on breast ultrasound performed 5–13 days after receipt of an mRNA COVID-19 vaccine. Consider vaccine-induced hyperplastic axillary adenopathy in differential diagnosis if unilateral axillary adenopathy identified on breast imaging in individuals who recently received an mRNA COVID-19 vaccine. Some experts suggest scheduling routine screening mammography or ultrasound prior to first dose of an mRNA COVID-19 vaccine or 4–6 weeks following second dose of the vaccine, if possible, and if this would not unduly delay appropriate care.

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 vaccine; some experts suggest obtaining detailed history regarding COVID-19 vaccination (date of vaccination, arm used for vaccine injection) to guide optimal follow-up and avoid unnecessary biopsies in patients undergoing such imaging.

### **Myocarditis and Pericarditis**

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; these reports suggest an increased risk of myocarditis and pericarditis following vaccination, particularly within 7 days following the second dose. Symptom onset typically within 2–7 days (range: 0–40 days) after receipt of a dose of an mRNA COVID-19 vaccine. Reported more frequently after the second vaccine dose than the first dose.

Data to date indicate myocarditis and pericarditis following vaccination with an mRNA COVID-19 vaccine occurred predominantly in male adolescents and young adults (range: 12–29 years of age). In most reported cases, patients were hospitalized and responded to medications and rest with rapid improvement or resolution of symptoms. Additional data needed regarding potential for long-term sequelae.

Consider the possibility of myocarditis and pericarditis in the differential diagnosis for adolescents or young adults with acute chest pain, shortness of breath, or palpitations. During initial evaluation of suspected cases, query the patient about prior COVID-19 vaccination and

pertinent medical, travel, and social history; in addition, consider assessing ECG, troponin levels, and inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate. Consider expert consultation regarding diagnosis, management, and follow-up.

### **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 deferring subsequent doses until additional safety data are available. ACIP states there may be certain circumstances when administration of a subsequent dose can be considered, taking into account the individual's personal risk of severe acute COVID-19 (e.g., age, underlying conditions), level of COVID-19 in the community and personal risk of infection, availability of additional data on risk of myocarditis or pericarditis in such situations, and availability of additional data on long-term outcomes. Those 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. FDA states that a decision to administer the Moderna COVID-19 vaccine to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances. ACIP states that any COVID-19 vaccine approved or authorized by FDA can be administered 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.

Inform individuals receiving an mRNA COVID-19 vaccine, especially males 12–29 years of age, 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 advise them to seek medical care if symptoms of myocarditis or pericarditis occur after vaccination.

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

### **Thrombocytopenia**

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) during post-authorization surveillance. As of February 4, 2021, >18 million doses of the Pfizer-BioNTech COVID-19 vaccine and >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 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 patient 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**

Base decision to administer or delay vaccination in an individual with a current or recent febrile illness 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 recommends that a risk assessment 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 deferring COVID-19 vaccination 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. There is no recommended minimum interval between SARS-CoV-2 infection and COVID-19 vaccination, but evidence to date suggests that risk of reinfection is low in the period after initial infection, but may increase with time due to waning immunity.

ACIP states that viral testing to assess for acute SARS-CoV-2 infection or serologic testing to assess for prior infection solely for the purpose of COVID-19 vaccination decision-making *not* recommended. (See Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals under Cautions.)

### **Individuals with Recent Exposure to SARS-CoV-2 Infection**

ACIP states that COVID-19 vaccines not currently recommended for outbreak management or for postexposure prophylaxis in individuals with a specific known exposure to SARS-CoV-2; postexposure vaccination is unlikely to be effective in preventing disease following such exposures. (See Limitations of Vaccine Effectiveness under Cautions.)

### **Individuals in the community or outpatient setting with a known COVID-19 exposure:**

ACIP states that such individuals should not seek COVID-19 vaccination until their quarantine period has ended since this avoids potentially exposing healthcare personnel and other individuals to SARS-CoV-2 during the vaccination visit and avoids diagnostic confusion between possible adverse effects of the vaccine and symptoms of COVID-19. This recommendation includes individuals with a known COVID-19 exposure after receiving the first dose of an mRNA COVID-19 vaccine but before receiving the second dose of the vaccine.

**Individuals residing in congregate healthcare settings (e.g., long-term care facilities) or congregate non-healthcare settings (e.g., correctional and detention facilities, homeless shelters) who have had a known COVID-19 exposure or are undergoing screening:** ACIP states that such individuals may receive COVID-19 vaccination since exposure and transmission of SARS-CoV-2 can occur repeatedly for long periods of time in these settings and healthcare personnel and other staff are already in close contact with residents in these settings. Those waiting for results of SARS-CoV-2 testing may receive COVID-19 vaccination if they do not have symptoms consistent with COVID-19. Individuals providing vaccination services should employ appropriate infection prevention and control procedures. Viral testing to assess for acute SARS-CoV-2 infection solely for the purpose of COVID-19 vaccination decision-making is *not* recommended.

**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 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 not available to date regarding 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 Specific Drugs under Drug Interactions.)

### **Individuals with a History of Multisystem Inflammatory Syndrome**

Data not available to date regarding safety and efficacy of COVID-19 vaccines in adults or children with a history of multisystem inflammatory syndrome (MIS-A or MIS-C, respectively). Mechanisms of MIS-A and MIS-C 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 patient, 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-A or MIS-C, considerations include clinical recovery from MIS-C or MIS-A (including return to normal cardiac function), personal risk of severe acute COVID-19 (e.g., age, underlying conditions), level of COVID-19 transmission in the community and personal risk of reinfection, lack of safety data regarding administration of COVID-19 vaccines following MIS-A or MIS-C, and timing of any immunomodulatory therapies.

Current evidence suggests that the risk of reinfection with SARS-CoV-2 is low in the months after initial infection, but may increase with time due to waning immunity. ACIP states that individuals with a history of MIS-A or MIS-C should consider deferring COVID-19 vaccination until they have recovered from their illness and for 90 days after the date MIS-A or MIS-C was diagnosed, recognizing that the risk of reinfection and, therefore, the benefit from vaccination might increase with time following the initial infection.

If MIS-A or MIS-C associated with a confirmed SARS-CoV-2 infection develops after receipt of a COVID-19 vaccine, consider referral to a specialist in infectious diseases, rheumatology, or cardiology. 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/ensuring-safety/monitoring/cisa/index.html>).

If MIS-A or MIS-C occurs following COVID-19 vaccination, report the case 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. ACIP does not state a preference for any specific COVID-19 vaccine in such individuals. Clinical trials of COVID-19 vaccines demonstrated that safety and efficacy profiles in individuals with some underlying medical conditions, including those that place them at increased risk for severe COVID-19, are similar to safety and efficacy profiles in those without comorbidities.

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

### **Individuals with Altered Immunocompetence**

FDA-approved or FDA-authorized mRNA COVID-19 vaccines (Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine) are not live vaccines and, therefore, can be safely administered to immunocompromised individuals.

Individuals with altered immunocompetence, including those receiving immunosuppressive therapy (see Specific Drugs under Interactions), may have diminished immune responses to vaccines, including the Moderna COVID-19 vaccine.

Clinical trial data indicate immunocompromised individuals (e.g., solid organ transplant recipients, those with lymphoid malignancies) may have reduced immune responses following a 2-dose vaccination series of an mRNA COVID-19 vaccine compared with those who are not immunocompromised. There also is evidence that vaccinated immunocompromised individuals may have a higher rate of breakthrough SARS-CoV-2 infections than vaccinated individuals in the general population.

Data from small studies 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 safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine in solid organ transplant recipients indicate the third dose is only moderately effective in increasing potentially protective antibody titers in such patients.

FDA EUA for the Moderna COVID-19 vaccine permits administration of a third dose of the vaccine at least 28 days after completion of the initial 2-dose vaccination series in individuals ≥18 years of age who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise.

ACIP states that, although clinical benefit of a third (additional) dose of an mRNA COVID-19 vaccine after an initial 2-dose vaccination series in immunocompromised individuals is still under investigation, the potential for increased immune response and the acceptable safety profile of mRNA COVID-19 vaccines support the recommendation for a third dose in individuals with *moderate to severe* immunocompromise resulting from a medical condition or receipt of immunosuppressive medications or treatments. For public health purposes, ACIP states that immunocompromised individuals are considered fully vaccinated ≥2 weeks after the second dose of the 2-dose primary vaccination series of an mRNA COVID-19 vaccine.

ACIP recommends that a third dose of the Moderna COVID-19 vaccine be considered after the initial 2-dose primary series for individuals with *moderate to severe* immunocompromise including, but not limited to, the following:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR) T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (CD4<sup>+</sup> T-cell counts <200 cells/mm<sup>3</sup>, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., prednisone dosage at least 20 mg daily or equivalent given for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor necrosis factor (TNF) blocking agents, and other biologic agents that are immunosuppressive or immunomodulatory

ACIP states that factors to consider when assessing the general level of immune competence include disease severity, duration, clinical stability, complications, comorbidities, and any potentially immunosuppressive treatment. Do not use age or place of residence alone (e.g., residence in a long-term care facility), independent of a patient's medical condition, to determine the level of immune competence because the balance of benefits and risks of a third primary dose for individuals who are not moderately to severely immunocompromised is currently unknown.

Counsel immunocompromised individuals, including those who receive a third dose of the Moderna COVID-19 vaccine, about the unknown safety profile and effectiveness of COVID-19 vaccines in immunocompromised populations and the potential for reduced immune responses. Advise them of the need to continue following all current CDC guidelines for fully vaccinated individuals (e.g., wearing a mask in certain settings with substantial or high levels of viral transmission) to protect themselves from COVID-19. Encourage close contacts of immunocompromised individuals to be vaccinated against COVID-19.

Antibody testing to assess for immunity to COVID-19 following COVID-19 vaccination in individuals with altered immunocompetence *not* recommended. (See Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals under Cautions.)

#### **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 that 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**

American Association for the Study of Liver Diseases (AASLD) released a consensus statement regarding use of COVID-19 vaccines in individuals with chronic liver disease or a liver transplant. These experts state vaccination against COVID-19 is strongly recommended because of 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) dose of the vaccine administered  $\geq 28$  days after the 2-dose primary series.

AASLD states that individuals with chronic liver disease receiving antiviral treatment for HBV or HCV infection and those receiving medical therapy for primary biliary cholangitis or autoimmune hepatitis should not discontinue such therapy when receiving COVID-19 vaccination. In addition, consider COVID-19 vaccination for patients with hepatocellular carcinoma undergoing locoregional or systemic therapy without interruption of treatment; however, those with recent infections or fever should not receive the vaccine until they are medically stable.

AASLD states that liver transplant candidates should receive COVID-19 vaccination prior to transplantation, whenever possible, to help ensure an adequate immune response. The optimal time for COVID-19 vaccination in previously unvaccinated liver transplant recipients is likely to be  $\geq 3$  months after transplant; however, vaccination may be given as early as 4 weeks after transplant if indicated based on ongoing community spread of SARS-CoV-2, especially in those at highest risk with other comorbid factors associated with severe COVID-19.

Reducing immunosuppressive therapy in liver transplant recipients solely as an effort to elicit an immune response to COVID-19 vaccination not recommended because of the risk of acute cellular rejection (ACR) with lower immunosuppression. AASLD recommends that COVID-19 vaccination be avoided in liver transplant recipients with active ACR, those being treated for ACR, and those receiving high daily doses of corticosteroids until the episode has resolved and the patient's baseline immunosuppression is reestablished.

Consult AASLD consensus statement 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 not reported in clinical trials evaluating mRNA COVID-19 vaccines.

ACIP states that individuals with a history of GBS may receive any COVID-19 vaccine approved or authorized by FDA, unless they have a contraindication to the vaccine. A history of GBS is not usually considered a contraindication or precaution to vaccination with most vaccines.

If GBS occurs following COVID-19 vaccination, report the case 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 not established, several cases of Bell's palsy reported in clinical trials in individuals who received the Moderna or the Pfizer-BioNTech COVID-19 vaccines.

Data from the ongoing 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, report the case to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

#### **Individuals with Increased Bleeding Risk**

Advise individuals who have bleeding disorders or are receiving anticoagulant therapy and/or their caregiver 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 patient's bleeding risk determines that the preparation can be administered IM with reasonable safety. In these cases, use a fine needle (23 gauge or smaller) to administer the vaccine and apply firm pressure to the injection site (without rubbing) for  $\geq 2$  minutes. In individuals receiving therapy for hemophilia, schedule IM vaccines for administration shortly after a dose of such therapy.

Individuals receiving anticoagulation therapy presumably have the same bleeding risk as those with clotting factor disorders and should follow the same guidelines for IM administration. If possible, schedule IM vaccines prior to use of an anticoagulant so that the patient'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 1–2 days after vaccination. This effect reported when the vaccine was given 2 weeks to 6 months or longer after last dermal filler injection; appears to be temporary and resolves with medical treatment, including corticosteroid therapy.

ACIP states that individuals who have received injectable dermal fillers may receive COVID-19 vaccination, unless they have a contraindication to the vaccine. However, advise such individuals to contact their healthcare provider for evaluation if they develop swelling at or near 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 not approved or authorized by FDA and/or not listed for emergency use by WHO. For the purposes of public health guidance, ACIP states that only individuals who have completed a primary series of a COVID-19 vaccine approved or authorized by FDA or listed by WHO for emergency use are considered fully vaccinated.

Limited data available regarding safety and efficacy of administering an FDA-approved or FDA-authorized COVID-19 vaccine to individuals who previously received a COVID-19 vaccine not approved or authorized in the US. ACIP states that such individuals may be offered a complete primary vaccination series using an FDA-approved or FDA-authorized COVID-19 vaccine. In such circumstances, the minimum interval between the last dose of the other COVID-19 vaccine and an FDA-approved or FDA-authorized COVID-19 vaccine is 28 days.

#### **Fully or Partially Vaccinated with a COVID-19 Vaccine Approved or Authorized by FDA**

Individuals vaccinated outside the US with a COVID-19 vaccine approved or authorized by FDA do *not* need any additional doses in the US if they previously received all the recommended primary doses of the vaccine.

If an individual in the US received the first dose of an FDA-approved or FDA-authorized COVID-19 vaccine outside the US and a 2-dose regimen is required, ACIP states the vaccination series does not need to be restarted; administer the second dose of the vaccine as close to the recommended interval as possible.

#### **Previously Received a COVID-19 Vaccine not Approved or Authorized by FDA but Listed for Emergency Use by WHO**

ACIP states that individuals who completed a COVID-19 vaccination series with a vaccine listed for emergency use by WHO do *not* need any additional doses using an FDA-approved or FDA-authorized COVID-19 vaccine.

May offer a complete vaccination series using an FDA-approved or FDA-authorized COVID-19 vaccine to individuals who partially completed a COVID-19 vaccination series outside the US with a vaccine listed for emergency use by WHO.

#### **Previously Received a COVID-19 Vaccine not Approved or Authorized by FDA or Listed for Emergency Use by WHO**

May offer a complete vaccination series using an FDA-approved or FDA-authorized COVID-19 vaccine to individuals who completed or partially completed a COVID-19 vaccination series outside the US with a vaccine not approved or authorized by FDA or listed for emergency use by WHO.

#### **Limitations of Vaccine Effectiveness**

May not protect all vaccine recipients against 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). Limited data

from the ongoing phase 3 trial evaluating the vaccine indicate that estimated vaccine efficacy is 80.2% following the first dose compared with 94.1% following the second dose. Counsel vaccine recipients on the importance of completing the 2-dose 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.

FDA states that data are too limited to date to assess the effect of the Moderna COVID-19 vaccine for prevention of asymptomatic SARS-CoV-2 infection (as measured by detection of the virus and/or detection of antibodies against non-vaccine antigens that would indicate infection rather than an immune response induced by the vaccine); additional evaluations are needed, including data from clinical trials and from use of the vaccine after issuance of the EUA.

FDA states that data are too limited to date to assess effect of the Moderna COVID-19 vaccine against transmission of SARS-CoV-2 from individuals who become infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 may translate to overall prevention of transmission in populations with high enough vaccine uptake; however, it is possible that if efficacy against asymptomatic infection were lower than efficacy against symptomatic infection, asymptomatic cases in combination with reduced mask-wearing and social distancing could result in significant continued transmission of the virus. Additional evaluations are needed, including data from clinical trials and from use of the vaccine after issuance of the EUA, to assess the effect of the vaccine in preventing virus shedding and transmission, particularly in individuals with asymptomatic infection.

Based on the unknown duration of vaccine-induced protection and unknown extent of protection against emerging SARS-CoV-2 variants, counsel 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 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. Consult these recommendations (available at the CDC website at <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html>) 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 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); such individuals should discuss the need for personal protective measures after COVID-19 vaccination with their healthcare provider.

Withholding COVID-19 vaccination due to concerns about efficacy against current or future SARS-CoV-2 viral variants not recommended.

If COVID-19 breakthrough infection occurs in an individual who has received one or more doses of a COVID-19 vaccine, prior receipt of the vaccine should not affect treatment decisions, including use of SARS-CoV-2-specific monoclonal antibodies, convalescent plasma, antivirals, or corticosteroids. For purposes of surveillance, breakthrough infections in fully vaccinated individuals are defined as detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected at least 14 days after completion of a primary vaccination series. If breakthrough infection occurs in a fully vaccinated individual and results in hospitalization or death, report the case to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

#### **Duration of Immunity**

Duration of protection against SARS-CoV-2 infection following completion of the 2-dose vaccination series of COVID-19 vaccine (Moderna) not fully evaluated.

#### **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. Inspect all vaccines on delivery and monitor during storage to ensure that recommended storage temperatures are maintained.

The Moderna COVID-19 vaccine 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. Do not administer vaccine that has been mishandled or has not been stored at the recommended temperatures. (See Storage under Stability.)

Contact the manufacturer at 866-663-3762 for guidance if there are concerns about mishandling or defective or damaged vaccine.

#### **EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting**

Safety and efficacy not established for uses authorized under the FDA EUA. The FDA issued an EUA that permits use of the Moderna COVID-19 vaccine for prevention of COVID-19

in individuals  $\geq 18$  years of age† when used as a 2-dose primary vaccination series and as a third dose† in the primary vaccination series in certain immunocompromised adults as specified in the EUA. (see Prevention of Coronavirus Disease 2019 [COVID-19] under Uses)

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

Monitor all vaccine recipients for immediate adverse reactions according to CDC (ACIP) guidelines. (See General under Dosage and Administration.)

Provide vaccine recipients or their caregivers 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. Reports to v-safe that indicate a medically important health impact are followed up by the CDC v-safe call center to collect additional information to complete a VAERS report. Information on v-safe is available at <https://www.cdc.gov/vsafe>.

**It is mandatory that vaccination providers administering the Moderna COVID-19 vaccine 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.** Can complete and submit VAERS reports online at <https://vaers.hhs.gov/reportevent.html> or by faxing to 877-721-0366; include the words "Moderna COVID-19 Vaccine EUA" in description section of the report. Obtain information on submitting a VAERS report by calling 800-822-7967 or emailing [info@vaers.org](mailto:info@vaers.org). To the extent feasible, also provide a copy of the VAERS form to the manufacturer (Moderna) at [ModernaPV@modernatx.com](mailto:ModernaPV@modernatx.com) (email), 866-599-1342 (fax), or 866-663-3762 (phone).

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

#### **Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals**

Results of SARS-CoV-2 viral tests (nucleic acid amplification or antigen tests) not affected by prior COVID-19 vaccination.

Use a test that specifically evaluates IgM/IgG to the nucleocapsid protein to assess 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).

Antibody testing *not* currently recommended to assess the need for COVID-19 vaccination in an unvaccinated individual or to assess for immunity to SARS-CoV-2 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, serologic correlates of protection against SARS-CoV-2 not established, and antibody testing does not evaluate cellular immune response, which may also play a role in vaccine-mediated protection. If antibody testing is performed following COVID-19 vaccination, do *not* administer additional doses of the same or different COVID-19 vaccine beyond those recommended based on results of antibody testing. If antibody testing was done after the first dose of an mRNA COVID-19 vaccine, complete the vaccination series regardless of antibody test results.

#### **Interpretation of Tuberculosis Tests in Vaccinated Individuals**

ACIP states do *not* delay COVID-19 vaccination 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.

If TST or IGRA required, perform such testing before, after, or during same visit that COVID-19 vaccine is administered. Although ACIP previously recommended delaying TST or IGRA testing until  $\geq 4$  weeks after completion of COVID-19 vaccination out of an abundance of caution to minimize potential theoretical interference between vaccination and TB testing, ACIP now states such testing can be administered without regard to timing of COVID-19 vaccination.

#### **Specific Populations**

##### **Pregnancy**

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

A developmental toxicity study in female rats did not reveal evidence of vaccine-related adverse effects on female fertility, fetal development, or postnatal development.

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 (ICU), 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 an increased risk of adverse pregnancy complications or outcomes, such as preeclampsia, coagulopathy, and stillbirth.

Post-authorization surveillance safety data are accumulating regarding COVID-19 vaccination during pregnancy and clinical trials evaluating safety and efficacy of COVID-19

vaccines in pregnant women are underway or planned. 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 nonpregnant individuals 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.

ACIP states vaccination against COVID-19 is recommended for pregnant women. These experts state that evidence regarding safety and efficacy of COVID-19 vaccines available from both animal and human studies indicates that benefits of vaccination against COVID-19 during pregnancy outweigh any known or potential risks. ACIP does not state a preference for any specific FDA-approved or FDA-authorized COVID-19 vaccine in pregnant women. For purposes of decisions regarding administration of the primary vaccination series, ACIP states consider pregnant and recently pregnant women (up until at least 42 days following the end of pregnancy) in the same group as individuals with underlying medical conditions.

ACIP states that pregnant women are eligible for and can receive COVID-19 vaccination; based on current knowledge, COVID-19 vaccines unlikely to pose a risk to pregnant women or the fetus. ACIP does not state a preference for any specific COVID-19 vaccine in such women.

ACOG recommends that pregnant women be vaccinated against COVID-19. When recommending the COVID-19 vaccine to pregnant women, ACOG suggests that clinicians review available data on risks and benefits of vaccination, including risks of not getting vaccinated, in the context of the individual patient's current health status and risk of exposure (e.g., possibility for exposure at work or home) and possibility for exposing high-risk household members. In addition, take into account the individual patient's values and perceived risk of various outcomes; 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 do not withhold Rh<sub>0</sub>(D) immune globulin when indicated in an individual who is planning to receive or recently received a COVID-19 vaccine. (See Specific Drugs under Interactions.)

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

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

Encourage women who receive a COVID-19 vaccine during pregnancy and those who become pregnant within 30 days after receiving a COVID-19 vaccine 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 *not* recommended before receiving a COVID-19 vaccine.

ACIP states vaccination against COVID-19 recommended for women currently trying to become 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 FDA-approved or FDA-authorized COVID-19 vaccines affect current or future fertility. FDA states there is no scientific evidence to suggest that Moderna COVID-19 vaccine could cause infertility in women. In addition, infertility 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**

Not known whether Moderna COVID-19 vaccine 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; breast-feeding women should discuss benefits and risks of vaccination with their healthcare providers.

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

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

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

#### **Pediatric Use**

Safety and efficacy of the Moderna COVID-19 vaccine not assessed in individuals <18 years of age.

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

#### **Geriatric Use**

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

At the time of FDA's safety and efficacy analysis of data from the ongoing phase 3 trial 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 those ≥65 years of age was 86.4% compared with 95.6% in those 18 to <65 years of age. No overall notable differences in safety profiles between participants ≥65 years of age and younger adults.

#### **Common Adverse Effects**

Local adverse effects in clinical trials: Injection site pain (92%), swelling (14.7%), erythema (10%).

Systemic adverse effects in clinical trials: Fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%).

Local and systemic adverse effects were usually reported within the first 1–2 days after a vaccine dose, 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 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.

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

At the time of FDA's safety analysis of data from the ongoing phase 3 trial evaluating a 2-dose regimen for the EUA, serious adverse events 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).

Severe allergic reactions (including anaphylaxis) and other hypersensitivity reactions (e.g., rash, pruritus, urticaria) reported rarely when the vaccine was administered outside of clinical trials. (See Hypersensitivity Reactions under Cautions.)

## **Interactions**

### **Vaccines**

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

Extensive experience with non-COVID-19 vaccines 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). Base decisions to administer a COVID-19 vaccine concomitantly with other vaccine(s) 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 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, give each parenteral vaccine at a different injection site and, if possible, separate injection sites by ≥1 inch. ACIP states that, although >1 vaccine can be given IM into the deltoid muscle in adolescents and adults, give COVID-19 vaccines and vaccines likely to cause a local reaction in different limbs, if possible.

### **Specific Drugs**

<b>Drug</b>	<b>Interaction</b>	<b>Comments</b>
<b>Antiviral agents</b>	Antiviral agents given at any interval before or after COVID-19 vaccination unlikely to impair development of vaccine-induced	



	protective antibody responses	
<b>COVID-19 convalescent plasma</b>	Data not available; not known whether prior receipt of such antibody therapy interferes with immune response to the vaccine	To avoid potential interference with vaccine immune response, ACIP recommends deferring COVID-19 vaccination for $\geq 90$ days after such antibody therapy based on estimated half-life of SARS-CoV-2 antibody therapies and evidence suggesting reinfection uncommon in first 90 days after initial infection; however, COVID-19 vaccination not contraindicated in those who received passive antibody therapy within the past 90 days and COVID-19 vaccine doses received $< 90$ days after receipt of passive antibody therapy do not need to be repeated  If COVID-19 subsequently develops in a vaccinated individual, ACIP states prior receipt of COVID-19 vaccine should not affect treatment decisions, including use of SARS-CoV-2 antibody therapies, or timing of such treatment
<b>Immune globulin and antibody therapies not specific for SARS-CoV-2 (e.g., immune globulin IV [IGIV], Rh<sub>0</sub>[D] immune globulin)</b>		May give COVID-19 vaccine concurrently with or at any interval before or after immune globulin or antibody therapies not specific for SARS-CoV-2; ACIP states there is no recommended minimum interval between receipt of antibody therapies not specific for SARS-CoV-2 and COVID-19 vaccination
<b>Immunosuppressive agents (e.g., cancer chemotherapy, corticosteroids, radiation)</b>	Possible decreased or suboptimal antibody responses to vaccines, including the Moderna COVID-19 vaccine  Data insufficient to date to inform optimal timing of COVID-19 vaccination for individuals planning to receive immunosuppressive therapies	ACIP states that individuals receiving immunosuppressive therapy may receive COVID-19 vaccination if they have no contraindications to the vaccine  Based on general best practices for vaccination of immunocompromised individuals, ACIP states COVID-19 vaccination should ideally be completed $\geq 2$ weeks before initiation or resumption of immunosuppressive therapies, whenever possible; consider individual's risks related

		to their underlying condition and response to the vaccine if making decisions to delay immunosuppressive therapy to complete COVID-19 vaccination
		Revaccination after immune competence regained not recommended in individuals who received COVID-19 vaccine during chemotherapy or treatment with other immunosuppressive agents
		Corticosteroids given topically or by local injection (e.g., intra-articular, intrabursal, or tendon injection): COVID-19 vaccines may be administered without regard to timing of corticosteroid administration
		If COVID-19 subsequently develops in a vaccinated individual, ACIP states prior receipt of COVID-19 vaccine should not affect treatment decisions, including use of corticosteroids, or timing of such treatment
<b>SARS-CoV-2-specific monoclonal antibodies (bamlanivimab and etesevimab, casirivimab and imdevimab, sotrovimab)</b>	Data not available; not known whether prior receipt of such antibody therapy interferes with immune response to the vaccine	To avoid potential interference with vaccine immune response, ACIP recommends deferring COVID-19 vaccination for $\geq 90$ days after such antibody therapy based on estimated half-life of SARS-CoV-2 antibody therapies and evidence suggesting reinfection uncommon in first 90 days after initial infection; however, COVID-19 vaccination not contraindicated in those who received passive antibody therapy within the past 90 days and COVID-19 vaccine doses received $< 90$ days after receipt of passive antibody therapy do not need to be repeated  If COVID-19 subsequently develops in a vaccinated individual, ACIP states prior receipt of COVID-19 vaccine should not affect treatment decisions, including use of SARS-CoV-2 antibody

## Stability

### Storage

#### Parenteral

##### Suspension, for IM Use

Supplied as a frozen suspension in multiple-dose vials that *must* be shipped and stored (long-term) at a temperature between -50 to -15°C.

Do *not* store the Moderna COVID-19 vaccine on dry ice or at temperatures less than -50°C.

If transport at -50 to -15°C not feasible, available data support transport of one or more thawed multiple-dose vials for up to 12 hours at 2–8°C when shipped using shipping containers that are qualified to maintain a temperature of 2–8°C and if such transport occurs under routine road and air transportation conditions with minimal shaking and vibration. Vials transported at 2–8°C should not be refrozen and should be stored at 2–8°C until use.

Store multiple-dose vials of the vaccine in the original carton to protect from light. Thawed vaccines may be handled in room light conditions.

Consult EUA fact sheet for healthcare providers for the Moderna COVID-19 vaccine and information provided by CDC and the manufacturer for information on storage, handling, and stability of the vaccine. Storage and handling information contained in the EUA fact sheet for healthcare providers supersedes storage and handling information on vaccine vials and carton labels. Various documents and videos describing shipping, storage, and handling requirements and procedures are available at the manufacturer's website at <https://www.modernatx.com/covid19vaccine-eua/providers/storage-handling>.

Prior to first use, may thaw and store multiple-dose vials of the Moderna COVID-19 vaccine in a refrigerator (2–8°C) for up to 30 days. May store unused (i.e., unopened) vials for up to 24 hours at 8–25°C.

After withdrawing first dose of vaccine from the multiple-dose vial, vial should be held between 2–25°C and *must* be discarded if not used within 12 hours after first vial entry.

Once thawed, do *not* refreeze.

Expiration dates are not marked on vials and cartons of the Moderna COVID-19 vaccine. Scan the QR code on the vial or carton to reach an online resource that provides the expiration date based on the lot number printed on the packaging. Alternatively, obtain expiration dates by entering the lot number at the manufacturer's website at <https://www.modernatx.com/covid19vaccine-eua/providers/vial-lookup>. Because it is possible that expiration dates may be extended as more stability data become available, contact the manufacturer prior to discarding vaccine to determine if the expiration date has been extended.

## Actions

- 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 clinical trials in healthy adults 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 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 the Moderna COVID-19 vaccine contains 100 mcg of mRNA encoding the S glycoprotein of SARS-CoV-2. Each dose also contains 4 different lipids (SM-102, PEG 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose.
- Does not contain preservatives; vial stoppers are not made with natural rubber latex.

## Advice to Patients

- Prior to administration of COVID-19 vaccine (Moderna), the vaccine recipient or their caregiver must be provided 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 may 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 they should continue to follow preventative measures (e.g., wearing a mask, physically distancing) to help prevent COVID-19. In addition, inform immunocompromised individuals that their close contacts should be vaccinated as appropriate.
- 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.
- Inform vaccine recipients or their caregivers that the vaccination provider cannot charge them for the vaccine dose, any out-of-pocket vaccine administration fees, or any other fees for COVID-19 vaccination. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (e.g., private insurance, Medicare, Medicaid, US Health Resources & Services Administration [HRSA] COVID-19 assistance program for non-insured recipients). Individuals who become aware of any potential violations of these requirements are encouraged to report them to the Office of the Inspector General, US Department of Health and Human Services by phone (800-HHS-TIPS) or online (<https://tips.oig.hhs.gov>).
- Inform vaccine recipients or their caregivers that they have the option to accept or refuse the vaccine.
- 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) 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. (See Contraindications under Cautions.)
- 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.

## 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† and as a third dose‡ in the primary

series in certain immunocompromised adults  $\geq 18$  years of age. 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**

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

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