

COVID-19 Vaccine, mRNA (Pfizer-BioNTech)

80:12 • Vaccines (AHFS primary)

Special Alerts:

On May 10, 2021, FDA reissued the emergency use authorization (EUA) for COVID-19 vaccine (Pfizer-BioNTech) to permit use of the vaccine in adolescents 12 through 15 years of age in addition to individuals 16 years of age and older. FDA reviewed efficacy and safety data from an ongoing phase 1, 2, 3 trial that has enrolled approximately 46,000 participants, including 2260 participants 12 through 15 years of age. Trial participants were randomized 1:1 to receive the Pfizer-BioNTech COVID-19 vaccine or saline control. FDA's analysis of available descriptive efficacy data from 1983 trial participants 12 through 15 years of age without evidence of SARS-CoV-2 infection prior to 7 days after the second vaccine dose confirm that the Pfizer-BioNTech COVID-19 vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose (no COVID-19 cases occurred in the vaccine group compared to 16 COVID-19 cases in the placebo group). FDA's review of available safety data for 2260 trial participants 12 through 15 years of age who were followed for a median of 2 months after receiving the second dose of the vaccine did not identify specific safety concerns that would preclude issuance of an EUA for this age group. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of the Pfizer-BioNTech COVID-19 vaccine in a subset of trial participants who had no serologic or virologic evidence of past SARS-CoV-2 infection confirm that the geometric mean antibody titer (GMT) in trial participants 12 through 15 years of age was noninferior to the GMT in participants 16 through 25 years of age. FDA reissued the EUA after concluding that it is reasonable to believe that the Pfizer-BioNTech COVID-19 vaccine may be effective in individuals 12 through 15 years of age and that it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of the vaccine outweigh known and potential risks for the prevention of COVID-19 in those 12 through 15 years of age.

For additional information, the Pfizer-BioNTech COVID-19 vaccine EUA letter of authorization (<https://www.fda.gov/media/144412/download>), EUA fact sheet for healthcare providers (<https://www.fda.gov/media/144413/download>), and EUA fact sheet for recipients and caregivers (<https://www.fda.gov/media/144414/download>) should be consulted.

The American Society of Health-System Pharmacists, Inc. represents that the information provided in the accompanying monograph was formulated with a reasonable standard of care, and in conformity with professional standards in the field. Readers are cautioned that COVID-19 Vaccine (Pfizer-BioNTech) is not an approved vaccine for coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2, but rather, is being investigated for and is currently available under an FDA emergency use authorization (EUA) for active immunization to prevent COVID-19 in individuals 12 years of age or older. The American Society of Health-System Pharmacists, Inc. makes no representations or warranties, express or implied, including, but not limited to, any implied warranty of merchantability and/or fitness for a particular purpose, with respect to the information contained in the accompanying monograph, and specifically disclaims all such warranties. Readers of this information are advised that ASHP is not responsible for the continued currency of the information, for any errors or omissions, and/or for any consequences arising from the use of the information contained in the monograph in any and all practice settings. Readers are advised that decisions regarding use of drugs are complex medical decisions requiring the independent, informed decision of an appropriate health care professional, and that the information contained in the monograph is provided for informational purposes only. The entire monograph for a drug should be reviewed for a thorough understanding of the drug's actions, uses and side effects. The American Society of Health-System Pharmacists, Inc. does not endorse or recommend the use of any drug. The information contained in the monograph is not a substitute for medical care.

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

Uses

■ Prevention of Coronavirus Disease 2019 (COVID-19)

COVID-19 vaccine (Pfizer-BioNTech) is an mRNA vaccine being investigated and used for the prevention of coronavirus disease 2019† (COVID-19) caused by SARS-CoV-2. The Pfizer-BioNTech COVID-19 vaccine is one of various COVID-19 vaccines being evaluated for the prevention of COVID-19.

Although efficacy and safety of COVID-19 vaccine (Pfizer-BioNTech) have not been definitively established, the vaccine is available under an FDA emergency use authorization (EUA) for active immunization to prevent COVID-19 in individuals 12 years of age or older.

The US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine for prevention of COVID-19. ACIP also issued interim recommendations regarding allocation of supplies of COVID-19 vaccines and interim considerations for phased implementation of COVID-19 vaccination and sub-prioritization among recommended populations in the US (available at the CDC website at <https://www.cdc.gov/vaccines/covid-19/phased-implementation.html> and <https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html>).

There currently are 3 different COVID-19 vaccines available for use in the US under FDA EUAs, including 2 mRNA vaccines (Pfizer-BioNTech COVID-19 vaccine and Moderna COVID-19 vaccine) and a viral-vectored vaccine (Janssen COVID-19 vaccine). ACIP does not state a preference for any specific currently authorized COVID-19 vaccine when the vaccines are used within the scope of their respective EUAs and states that individuals should be encouraged to receive the earliest vaccine available to them. However, currently available COVID-19 vaccines are *not* interchangeable with each other. (See Dosage under Dosage and Administration.)

Emergency Use Authorization

On December 11, 2020, FDA issued an EUA that permitted use of COVID-19 vaccine (Pfizer-BioNTech) to prevent COVID-19 in individuals 16 years of age or older. FDA reissued the EUA for the Pfizer-BioNTech COVID-19 vaccine on May 10, 2021 to permit use of the vaccine in individuals 12 years of age or older.

The EUA requires that the vaccine be administered by vaccination providers using a 2-dose vaccination series as described in the EUA (see 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 (e.g., requirements concerning obtaining, tracking, and handling vaccine) and requirements concerning reporting of vaccine administration data to CDC and state/local jurisdiction's Immunization Information System (IIS) or other designated systems.

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

Issuance of the EUA for COVID-19 vaccine (Pfizer-BioNTech) was based on FDA review of safety and efficacy data from an ongoing phase 1, 2, 3 clinical trial that included approximately 44,000 individuals randomized 1:1 to receive the vaccine or saline placebo. (See Clinical Experience under Uses.)

The EUA for the Pfizer-BioNTech 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 the risks of this unapproved vaccine, the EUA requires that vaccination providers administering the Pfizer-BioNTech COVID-19 vaccine comply with certain mandatory requirements. These requirements include providing the recipient or caregiver with information consistent with the EUA fact sheet for recipients and caregivers and 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.)

For additional information, the Pfizer-BioNTech COVID-19 vaccine EUA letter of authorization, EUA fact sheet for healthcare providers, and EUA fact sheet for recipients and caregivers should be consulted.

Clinical Experience

Efficacy and safety of COVID-19 vaccine (Pfizer-BioNTech) for the prevention of COVID-19 are being evaluated in an ongoing multinational, randomized, double-blind, placebo-controlled, phase 1, 2, 3 trial (NCT04368728; C45910001; study 2). At the time of FDA's efficacy review of the vaccine for the EUA, the efficacy analysis population had been followed for a median of approximately 2 months after the second dose, and data for study participants who had no evidence of prior SARS-CoV-2 infection at the time of enrollment indicated that the Pfizer-BioNTech COVID-19 vaccine was 95% effective in preventing COVID-19 occurring at least 7 days after the second dose of the 2-dose vaccination series compared with placebo.

Based on results of the dose-escalation phase 1 portion of study 2 that evaluated 3 different dosages of the Pfizer-BioNTech COVID-19 vaccine in healthy adults 18 years of age or older, a 2-dose regimen consisting of 30-mcg doses of the vaccine was selected for the phase 2/3 portion of the trial. In phase 2/3, enrollees were randomized 1:1 to receive 2 IM doses given 21 days apart of the Pfizer-BioNTech COVID-19 vaccine (30 mcg for each dose) or saline placebo, and randomization was stratified into 3 age groups (12–15, 16–55, or 56 years of age and older) with a minimum of 40% of enrollees in the 56 years of age and older group. Healthy individuals and those with stable chronic disease (i.e., disease not requiring significant change in therapy or

hospitalization for worsening disease during the 6 weeks before enrollment), including but not limited to human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV) infection, were eligible for enrollment; individuals who had immunocompromising diseases or were receiving immunosuppressive therapy and those with a previous clinical or microbiologic diagnosis of COVID-19 were excluded. The primary efficacy end point is efficacy of the vaccine against confirmed COVID-19 with onset at least 7 days after the second dose of the 2-dose vaccination series in participants who had no serologic or virologic evidence of SARS-CoV-2 infection prior to 7 days after the second dose; the second primary end point is efficacy in participants with or without evidence of SARS-CoV-2 infection prior to 7 days after the second dose. Among the 36,523 participants 16 years of age or older in the phase 2/3 portion of the trial who had no evidence of existing or prior SARS-CoV-2 infection (18,198 in the vaccine group and 18,325 in the placebo group), there were 8 cases of COVID-19 with onset at least 7 days after the second dose among vaccine recipients and 162 cases among placebo recipients; this corresponds to 95% vaccine efficacy. Among the 40,137 participants 16 years of age or older with or without evidence of SARS-CoV-2 infection prior to 7 days after the second dose (19,965 in the vaccine group and 20,172 in the placebo group), there were 9 cases of COVID-19 with onset at least 7 days after the second dose among vaccine recipients and 169 cases among placebo recipients; this corresponding to 94.6% vaccine efficacy.

Additional primary efficacy analyses among subgroups defined by age, sex, race, ethnicity, and presence of medical conditions associated with increased risk for severe COVID-19 (e.g., obesity, chronic lung disease, significant cardiac disease, diabetes mellitus, hypertension, liver disease) indicated that vaccine efficacy in these subgroups generally was consistent with that observed in the overall population.

Dosage and Administration

■ General

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

Prior to administration of each dose of the Pfizer-BioNTech COVID-19 vaccine, all individuals should be screened for contraindications and precautions to vaccination. Those with a contraindication should not receive the Pfizer-BioNTech COVID-19 vaccine. (See Contraindications and see Warnings/Precautions under Cautions.)

All individuals who receive a COVID-19 vaccine should be monitored for immediate adverse reactions according to CDC (ACIP) guidelines. When individuals with no contraindications to vaccination with the Pfizer-BioNTech COVID-19 vaccine receive the vaccine, ACIP states that 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 should be observed for 30 minutes after receiving the vaccine, and that all other individuals should be observed for 15 minutes. A longer period of observation may be indicated for some individuals based on clinical concern (e.g., vaccinee develops pruritus and swelling confined to the injection site during their observation period). Vaccine recipients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site. (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. Appropriate measures should be taken to decrease the 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, the patient should be observed until symptoms resolve.

COVID-19 vaccine (Pfizer-BioNTech) is administered in a series of 2 doses given 3 weeks (21 days) apart. (See Dosage under Dosage and Administration.) At the time that the first dose of the Pfizer-BioNTech COVID-19 vaccine is administered, vaccine recipients or their caregivers should be given a vaccination record card that provides the date when the recipient needs to return for the second dose of the vaccine and counseled on the importance of completing the 2-dose vaccination series to optimize protection against COVID-19.

Vaccine recipients or their caregivers should be provided with information on, and encouraged to participate in, CDC's v-safe program, a voluntary smartphone-based tool that uses text messaging and web surveys to monitor for adverse effects in individuals who have received a COVID-19 vaccine. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Prior to vaccination, vaccine recipients or their caregivers should be counseled about local and systemic adverse effects that may occur following vaccination. (See

Cautions and see Advice to Patients.) Unless an individual has a contraindication to vaccination with an mRNA COVID-19 vaccine (see Contraindications under Cautions), ACIP recommends that vaccinees should be encouraged to complete the 2-dose vaccination series of the Pfizer-BioNTech COVID-19 vaccine even if they experience local or systemic adverse effects following the first dose since this optimizes protection.

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

Individuals who receive COVID-19 vaccine (Pfizer-BioNTech) should be counseled to continue to follow all current guidance to protect themselves and others. This includes wearing a mask, staying at least 6 feet away from others, avoiding crowds, avoiding poorly ventilated spaces, covering coughs and sneezes, washing hands frequently, following CDC travel guidance, and following any applicable workplace or school guidance. This recommendation is based on the currently limited information on the extent to which vaccination may reduce viral transmission in the general population, the unknown duration of vaccine-induced protection, and the unknown extent of protection against emerging SARS-CoV-2 variants. (See Limitations of Vaccine Effectiveness under Cautions.)

■ Administration

COVID-19 vaccine (Pfizer-BioNTech) is administered *only* by IM injection into the deltoid.

Data are not available regarding concomitant administration of COVID-19 vaccine (Pfizer-BioNTech) with other vaccines. ACIP recommends that the Pfizer-BioNTech COVID-19 vaccine *not* be administered simultaneously with or within 14 days of any other vaccine. (See Vaccines under Drug Interactions.)

IM Injection

COVID-19 vaccine (Pfizer-BioNTech) is supplied as a frozen suspension concentrate in multiple-dose vials.

The frozen Pfizer-BioNTech COVID-19 vaccine suspension concentrate *must* be shipped at ultra-low temperatures (between -80 to -60°C) and stored frozen at specific temperatures. (See Stability.)

Prior to use, the frozen Pfizer-BioNTech COVID-19 vaccine concentrate *must* be thawed and then diluted with 0.9% sodium chloride injection *only*.

To administer a dose of the thawed and diluted Pfizer-BioNTech COVID-19 vaccine, 0.3 mL of the vaccine should be withdrawn from the vial using aseptic technique and an appropriate syringe and needle and administered immediately. A 1-mL low dead-volume syringe and needle is preferred for administration of the vaccine; a standard 1-mL syringe can be used if a low dead-volume syringe is not available.

Each multiple-dose vial of thawed and diluted Pfizer-BioNTech COVID-19 vaccine provides six 0.3-mL doses when low dead-volume syringes and needles are used to extract doses from the vial. If standard syringes and needles are used, the volume of remaining vaccine may be insufficient to extract a sixth dose from the vial. Irrespective of the type of syringe and needle used, each dose *must* contain 0.3 mL of vaccine.

FDA states that it is acceptable to use every full dose obtainable from the multiple-dose vial despite the fact that some vial labels and cartons may state that the vial contains five 0.3-mL doses. However, because the vaccine does not contain preservatives, it is critical that any vaccine remaining in the vial that does not constitute a full 0.3-mL dose should be discarded and should *not* be pooled with vaccine from other vials to create a dose.

Thawing.

Frozen COVID-19 vaccine (Pfizer-BioNTech) suspension concentrate may be thawed either in a refrigerator (2–8°C) or at room temperature (up to 25°C).

Thawing in a refrigerator (2–8°C): A full carton or tray containing 25 or 95 vials of frozen suspension concentrate may take up to 2 or 3 hours, respectively, to thaw; less time is required to thaw fewer vials. The vials of thawed vaccine may be stored in the refrigerator for up to 5 days (120 hours) before dilution.

Thawing at room temperature (up to 25°C): Vial(s) should be allowed to sit at room temperature for 30 minutes to thaw and may be kept at room temperature for up to a total of 2 hours. After 2 hours at room temperature, the thawed vaccine should be diluted or placed in a refrigerator (2–8°C).

Thawed COVID-19 vaccine (Pfizer-BioNTech) suspension concentrate should appear as a white to off-white suspension and may contain white to off-white opaque amorphous particles. The thawed vaccine should *not* be used if it is discolored or contains other particles.

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

Dilution.

Thawed COVID-19 vaccine (Pfizer-BioNTech) suspension concentrate *must* equilibrate to room temperature prior to dilution and *must* be diluted within 2 hours after reaching room temperature.

Prior to dilution, vial(s) containing the thawed vaccine suspension concentrate should be gently inverted 10 times and should *not* be shaken.

Using aseptic technique, 1.8 mL of 0.9% sodium chloride injection should be withdrawn into a 3- or 5-mL transfer syringe (21-gauge needle or narrower) and injected into the vial of thawed Pfizer-BioNTech COVID-19 vaccine suspension concentrate; no more than 1.8 mL of diluent should be added to the vial. To equalize vial pressure, 1.8 mL of air should be withdrawn into the empty diluent syringe before removing the needle from the vial. Other diluents (e.g., bacteriostatic 0.9% sodium chloride injection) should *not* be used.

After the 0.9% sodium chloride diluent has been added, the vial should be gently inverted 10 times to mix and should *not* be shaken.

Following dilution, COVID-19 vaccine (Pfizer-BioNTech) should appear as an off-white suspension and should *not* be used if it is discolored or contains particulates.

The date and time of dilution *must* be recorded on the vaccine vial.

Vials containing diluted COVID-19 vaccine (Pfizer-BioNTech) may be stored between 2–25°C, but *must* be used within 6 hours after dilution (regardless of storage temperature). Unused diluted vaccine remaining in vials should be discarded if not used within 6 hours after dilution.

Dosage

COVID-19 vaccine (Pfizer-BioNTech) is administered in a series of two 0.3-mL doses given 3 weeks (21 days) apart. Each 0.3-mL dose contains 30 mcg of modRNA (see Description).

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

Clinicians should ensure that individuals who receive the first dose of the Pfizer-BioNTech COVID-19 vaccine receive a second dose of the same vaccine at the recommended interval to complete the vaccination series.

The EUA that permits use of COVID-19 vaccine (Pfizer-BioNTech) specifies an interval of 3 weeks (21 days) between the 2 vaccine doses. ACIP states that individuals should not be scheduled to receive the second dose of the vaccine earlier than 3 weeks after the first dose; however, a second dose administered within a grace period of 4 days earlier than the recommended date is still considered valid. If it is not feasible to adhere to the recommended interval and a delay in vaccination is unavoidable, ACIP states that the second dose may be administered up to 6 weeks (42 days) after the first dose; only limited data are available regarding efficacy if the second dose of an mRNA COVID-19 vaccine is administered more than 6 weeks after the first dose.

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

Safety and efficacy of a mixed vaccination series of mRNA COVID-19 vaccines have not been evaluated, and individuals who receive a dose of the Pfizer-BioNTech COVID-19 vaccine should complete the series using the same vaccine. Every effort should be made to determine which mRNA COVID-19 vaccine was used for the 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 the first dose cannot be determined or is no longer available, any available mRNA COVID-19 vaccine may be administered 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 that it is preferable to delay the second dose (up to 6 weeks) 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 in such situations (or inadvertently), ACIP states that no additional doses of either vaccine are recommended at this time.

Safety and efficacy regarding use of the viral-vectored vaccine (Janssen COVID-19 vaccine) after a dose of an mRNA COVID-19 vaccine have not been 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), a single dose of the Janssen COVID-19 vaccine administered at least 28 days after the first dose of mRNA COVID-19 vaccine may be considered. (See Hypersensitivity Reactions under Cautions.) An individual who receives a dose of an mRNA COVID-19 vaccine followed by a single dose of the Janssen COVID-19 vaccine under such exceptional circumstances should be considered to have received valid, single-dose vaccination with Janssen COVID-19 vaccine, not a mixed vaccination series.

All vaccine administration errors and deviations from the currently recommended dosage and vaccination schedule should be reported 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 how to prevent and report COVID-19 vaccine administration errors and recommendations for specific actions to take if an administration error or deviation from the recommended vaccination schedule occurs are available at the CDC website at <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>.

Adult Dosage

The FDA EUA that permits use of COVID-19 vaccine (Pfizer-BioNTech) for the prevention of COVID-19† (see Emergency Use Authorization under Uses) states that adults 18 years of age or older should receive two 0.3-mL doses of the vaccine administered 3 weeks (21 days) apart.

Pediatric Dosage

Adolescents 12 Years of Age or Older.

The FDA EUA that permits use of COVID-19 vaccine (Pfizer-BioNTech) for the prevention of COVID-19† (see Emergency Use Authorization under Uses) states that adolescents 12 years of age or older should receive two 0.3-mL doses of the vaccine administered 3 weeks (21 days) apart.

Cautions

■ Contraindications

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

ACIP considers the following to be contraindications to vaccination with *both* mRNA COVID-19 vaccines (Pfizer-BioNTech COVID-19 vaccine and Moderna 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.

Although immediate allergic reactions have not been reported to date in clinical trials evaluating COVID-19 vaccine (Pfizer-BioNTech), severe allergic reactions, including anaphylaxis, have been reported rarely following administration of mRNA COVID-19 vaccines during mass vaccination campaigns 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 occurring between December 14–23, 2020 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 a documented history of allergies or allergic reactions to drugs or medical products, foods, or insect stings (7 with a history of anaphylaxis, including one after receipt of a dose of rabies vaccine and another after receipt of influenza vaccine). The median interval from receipt of the vaccine dose to onset of anaphylaxis symptoms was 13 minutes (range: 2–150 minutes); 15 of the 21 individuals with anaphylaxis (71%) had onset of symptoms within 15 minutes after receiving the dose and 19 (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 a documented history of allergies or allergic reactions to drugs, contrast media, or food (5 with a history of anaphylaxis). The median interval from receipt of the vaccine dose to onset of symptoms was 7.5 minutes (range: 1–45 minutes); 9 of the 10 individuals had onset within 15 minutes and one had onset after 30 minutes. All 10 individuals were treated with epinephrine. No fatalities from anaphylaxis were reported; 4 individuals were treated in an emergency department and the other 6 were hospitalized (including 5 in an intensive care unit).

Between December 14–23, 2020, VAERs identified 83 cases of nonanaphylactic allergic reactions after administration of the first dose of the Pfizer-BioNTech COVID-19 vaccine; 72 of these cases (87%) were classified as nonserious and 56 of the cases (67%) included a documented history of allergies or allergic reactions. The median interval from receipt of the vaccine dose to onset of such symptoms was 12 minutes (range: less than 1 minute to 20 hours); in 61 cases (85%), onset of symptoms occurred within 30 minutes. Hypersensitivity reactions reported with the vaccine have included rash, pruritus, urticaria, itchy/scratchy sensations in the throat, angioedema, and mild respiratory symptoms.

Individuals with a history of significant allergic reaction to any vaccine or to any component of the Pfizer-BioNTech COVID-19 vaccine were excluded from participating in clinical trials; however, those with a history of other significant allergic reactions were not excluded. FDA independently conducted a standard MedDRA

queries (SMQs) review of data from the safety population of the ongoing randomized, placebo-controlled, phase 2/3 trial evaluating the Pfizer-BioNTech vaccine to evaluate for constellations of unsolicited adverse events using preferred terms that could represent various diseases and conditions including, but are not limited to, allergic, neurologic, inflammatory, and autoimmune conditions. The SMQs revealed a slight numerical imbalance of adverse events potentially representing allergic reactions, with more hypersensitivity-related adverse events reported in the vaccine group than the placebo group (0.63% and 0.51%, respectively).

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

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

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

History of severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components (e.g., PEG):

ACIP considers this a **contraindication** to vaccination with both the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine. ACIP states that consideration can be given to using an alternative COVID-19 vaccine (Janssen COVID-19 vaccine) in such individuals. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/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 have not been 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), a single dose of the Janssen COVID-19 vaccine may be considered at a minimum interval of 28 days after the dose of mRNA COVID-19 vaccine. (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 Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine. ACIP states that consideration can be given to using an alternative COVID-19 vaccine (Janssen COVID-19 vaccine) in such individuals. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/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 have not been 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), a single dose

of the Janssen COVID-19 vaccine may be considered at a minimum interval of 28 days after the dose of the mRNA COVID-19 vaccine. (See Dosage under Dosage and Administration.)

History of polysorbate allergy: ACIP considers this a **precaution** to vaccination with both the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine. ACIP states that polysorbate allergy is a contraindication to vaccination with the Janssen COVID-19 vaccine and that use of an mRNA COVID-19 vaccine (Pfizer-BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine) can be considered in such individuals. However, polysorbates are structurally related to PEG and there is potential for cross-reactive hypersensitivity. Consultation with an allergist-immunologist should be considered to help determine if the individual with polysorbate allergy can safely receive an mRNA COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (<https://www.cdc.gov/vaccinesafety/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), the vaccine should be administered *only* in an appropriate setting under the supervision of a healthcare provider experienced in the management of severe allergic reactions.

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

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

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

History of delayed-onset local reactions (e.g., erythema, induration, pruritus) around the injection site area after the first dose of an mRNA COVID-19 vaccine:

ACIP states that these local reactions are **not** a contraindication or precaution for administration of the second dose of the mRNA COVID-19 vaccine. Such individuals should receive the second dose using the same mRNA COVID-19 vaccine used for the first dose at the recommended interval, preferably in the opposite arm.

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

When a COVID-19 vaccine, including the Pfizer-BioNTech COVID-19 vaccine, is administered to individuals without a contraindication to such vaccines, ACIP states that 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 should be observed for 30 minutes after the vaccine dose and that all other individuals should be observed for 15 minutes. In addition, vaccine recipients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site.

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

ACIP interim guidance regarding 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>).

Concomitant Illness

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

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

Individuals with Prior SARS-CoV-2 Infection.

Available data suggest that COVID-19 vaccines can be given safely to individuals with evidence of *prior* SARS-CoV-2 infection. ACIP states that COVID-19 vaccination should be offered to individuals regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection.

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

Individuals with Current SARS-CoV-2 Infection.

ACIP recommends that COVID-19 vaccination be deferred in individuals with known *current* SARS-CoV-2 infection until they have recovered from the acute illness (if symptomatic) and until criteria for discontinuance of isolation have been met. This recommendation applies to individuals who experience SARS-CoV-2 infection before receiving any doses of COVID-19 vaccine and those who experience SARS-CoV-2 infection after receiving the first dose of an mRNA COVID-19 vaccine but before receiving the second dose of the vaccine. While there is no recommended minimum interval between SARS-CoV-2 infection and COVID-19 vaccination, evidence to date suggests that the risk of reinfection is low in the months after initial infection, but may increase with time due to waning immunity. If vaccine supply is limited, ACIP states that individuals with recent documented acute SARS-CoV-2 infection may choose to temporarily delay COVID-19 vaccination, if desired, recognizing that the risk of reinfection and need for vaccination may increase with time following the initial infection.

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 is *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 are 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 to avoid potentially exposing healthcare personnel and other individuals to SARS-CoV-2 during the vaccination visit. This recommendation also applies to 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) with a known COVID-19 exposure: 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. Individuals providing vaccination services should employ appropriate infection prevention and control procedures.

Residents in congregate settings (healthcare and non-healthcare) with a known COVID-19 exposure waiting for results of SARS-CoV-2 testing: ACIP states that such individuals 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. (See Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals under Cautions.)

Individuals with Underlying Medical Conditions

ACIP states that individuals with altered immunocompetence or certain underlying medical conditions may receive any authorized COVID-19 vaccine, unless they have a contraindication to the vaccine. Clinical trials of COVID-19 vaccines have 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.

Individuals with Altered Immunocompetence.

Individuals with altered immunocompetence, including those receiving immunosuppressive therapy (see Immunosuppressive Agents under Drug Interactions), may have diminished immune responses to vaccines, including the Pfizer-BioNTech COVID-19 vaccine.

Although some individuals with altered immunocompetence (e.g., stable HIV infection) have been included in the ongoing randomized, placebo-controlled, phase 2/3 trial evaluating the Pfizer-BioNTech COVID-19 vaccine, the number of such individuals was insufficient to evaluate safety and efficacy of the vaccine in such populations.

ACIP states that individuals with HIV infection or other immunocompromising conditions and individuals receiving immunosuppressive therapies may be at increased risk for severe COVID-19 and, although data are not currently available to establish safety and efficacy in such individuals, they may receive any authorized COVID-19 vaccine, unless they have a contraindication to the vaccine. However, such individuals should be counseled about the unknown safety profile and effectiveness of COVID-19 vaccines in immunocompromised populations, as well as the potential for reduced immune responses and the need to continue following all current guidelines to protect themselves from COVID-19.

Antibody testing to assess for immunity to COVID-19 following COVID-19 vaccination in individuals with altered immunocompetence is *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 authorized COVID-19 vaccine, unless they have a contraindication to the vaccine. Although data are not currently available regarding the safety and efficacy of COVID-19 vaccines in individuals with autoimmune conditions, such individuals were not excluded from clinical trials evaluating mRNA COVID-19 vaccines and these trials showed no imbalances in the occurrence of symptoms consistent with autoimmune conditions or inflammatory disorders in trial participants who received a COVID-19 vaccine compared with those who received placebo.

Individuals with Liver Disease.

The American Association for the Study of Liver Diseases (AASLD) has released a consensus statement regarding use of COVID-19 vaccines in individuals who have chronic liver disease or are liver transplant recipients.

Although safety and efficacy data regarding use of COVID-19 vaccines in individuals with chronic liver disease are limited and additional studies are needed, safety and efficacy of the vaccines in such individuals are expected to be similar to the general population. AASLD states that individuals with chronic liver disease who are receiving antiviral treatment for hepatitis B virus (HBV) or hepatitis C virus (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, patients with hepatocellular carcinoma undergoing locoregional or systemic therapy should be considered for COVID-19 vaccination without interruption of treatment.

Although solid organ transplant recipients, including liver transplant recipients, were not included in clinical trials of COVID-19 vaccines and efficacy and safety in such individuals are not known, AASLD states that liver transplant candidates should receive COVID-19 vaccination prior to transplantation, whenever possible, to help ensure an adequate immune response. The best time for COVID-19 vaccination in previously unvaccinated liver transplant recipients is likely to be at least 3 months after transplant; however, vaccination may be given as early as 6 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.

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

Individuals with a History of Guillain-Barré Syndrome.

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

ACIP states that individuals with a history of Guillain-Barré syndrome (GBS) may receive COVID-19 vaccination, 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, the case should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Individuals with a History of Bell's Palsy.

Although a causal relationship has not been established, several cases of Bell's palsy have been reported in clinical trials in individuals who received the Pfizer-BioNTech COVID-19 vaccine or the Moderna COVID-19 vaccine.

Data from the ongoing randomized, double-blind, placebo-controlled, phase 2/3 trial evaluating the Pfizer-BioNTech COVID-19 vaccine identified 4 cases of Bell's palsy (facial paralysis) in participants who received the vaccine. Onset of facial paralysis in one individual occurred on day 37 after the first vaccine dose (participant did not receive the second dose), and onset occurred on days 3, 9, or 48 after the second dose in the other individuals. No cases of Bell's palsy were reported in the placebo group. FDA stated that these 4 cases in the vaccine group do not represent a frequency greater than that expected in the general population.

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

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

Individuals with Increased Bleeding Risk.

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

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

Individuals receiving anticoagulation therapy presumably have the same bleeding risk as patients with clotting factor disorders and should follow the same guidelines for IM administration. If possible, IM vaccines could be scheduled prior to use of an anticoagulant so that the 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 within 1–2 days after vaccination. This effect has been reported when the vaccine was administered 2 weeks to 6 months or longer after the last dermal filler injection, and appears to be temporary and resolves with medical treatment, including corticosteroid therapy. A similar inflammatory reaction at the site of dermal filler injections (lips, cheeks, tear troughs) was reported in at least one unvaccinated individual who was diagnosed with COVID-19 approximately 2 weeks after their last dermal filler injection and has been reported after natural influenza-like illness. Although the mechanism of these reactions is not known, it has been suggested that localized swelling at the site of dermal filler injection may be due to an inflammatory reaction resulting from an interaction between the immune response after vaccination and the dermal filler.

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

Lymphadenopathy

Lymphadenopathy has been reported in clinical trials evaluating COVID-19 vaccine (Pfizer-BioNTech). At the time that FDA's safety and efficacy analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 2/3 trial evaluating the Pfizer-BioNTech COVID-19 vaccine was performed for the EUA, lymphadenopathy was reported in 0.3% of vaccine recipients. Lymphadenopathy lasted an average of 10 days, occurred more frequently in the vaccine group than the placebo group, and was temporally associated with the vaccine.

Cases of unilateral axillary adenopathy, including palpable axillary mass, have been identified through self-detection or incidentally on breast imaging in individuals who received an mRNA COVID-19 vaccine outside of clinical trials. In some reported cases, axillary adenopathy on the same side as the vaccination site was seen on breast ultrasound performed 5–13 days after receipt of an mRNA COVID-19 vaccine. Vaccine-induced hyperplastic axillary adenopathy should be considered in the differential diagnosis if unilateral axillary adenopathy is identified on breast imaging in individuals who recently received an mRNA COVID-19 vaccine.

Limitations of Vaccine Effectiveness

COVID-19 vaccine (Pfizer-BioNTech) may not protect all vaccine recipients against COVID-19.

The Pfizer-BioNTech COVID-19 vaccine is administered in a series of 2 doses given 3 weeks (21 days) apart (see Dosage under Dosage and Administration). Data from the ongoing randomized, double-blind, placebo-controlled, phase 2/3 trial evaluating COVID-19 vaccine (Pfizer-BioNTech) indicate that estimated vaccine efficacy is 52% following the first dose compared with 95% following the second dose. Vaccine recipients should be counseled 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 Pfizer-BioNTech 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 use of the vaccine after issuance of the EUA.

FDA states that data are too limited to date to assess the effect of Pfizer-BioNTech 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 currently limited information on the extent to which vaccination may reduce viral transmission in the general population, the unknown duration of vaccine-induced protection, and the unknown extent of protection against emerging SARS-CoV-2 variants, individuals who receive COVID-19 vaccination should be counseled to continue to follow all current guidance to protect themselves and others. This includes wearing a mask, staying at least 6 feet away from others, avoiding crowds, avoiding poorly ventilated spaces, covering coughs and sneezes, washing hands frequently, following CDC travel guidance, and following any applicable workplace or school guidance.

CDC has issued interim public health recommendations for individuals who are fully vaccinated against COVID-19 (defined as at least 2 weeks after completion of a 2-dose vaccination series of the Pfizer-BioNTech COVID-19 vaccine or the Moderna COVID-19 vaccine or at least 2 weeks after a single dose of the Janssen COVID-19 vaccine). These recommendations (available at the CDC website at <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html>) should be consulted for information on precautionary measures that fully vaccinated individuals should take in various social situations and/or following exposure to someone with suspected or confirmed COVID-19.

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

If an individual is fully vaccinated against COVID-19 and tests positive for SARS-CoV-2, healthcare providers and local health departments are encouraged to request that the specimen be held and the case reported to the state health department. CDC will work with the state health department to collect information about the case. In addition, information about such cases should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Duration of Immunity

The duration of protection against SARS-CoV-2 infection following completion of the 2-dose vaccination series of COVID-19 vaccine (Pfizer-BioNTech) has not been fully evaluated.

Because available trial data have a limited length of follow-up to date, it is not possible at this time to assess sustained efficacy over a period longer than 2 months.

ACIP states that the need for and timing of booster doses of COVID-19 vaccines have not been established. Additional vaccine doses beyond those recommended for a complete, valid vaccination series (see Dosage under Dosage and Administration) are *not* recommended at this time. Recommendations on revaccination or additional doses of COVID-19 vaccines may be updated when additional information is available.

Improper Storage and Handling

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

COVID-19 vaccine (Pfizer-BioNTech) 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. (See Stability.)

If there are concerns about mishandling, including inadvertent temporary temperature excursions, the manufacturer should be contacted at 800-666-7248 or 877-829-2619 for guidance.

EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting

Safety and efficacy of COVID-19 vaccine (Pfizer-BioNTech) have not been established. The FDA issued an EUA that permits use of the vaccine for the prevention of COVID-19† in individuals 12 years of age or older when administered according to the 2-dose vaccination series specified in the EUA. (See Emergency Use Authorization under Uses.)

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

All vaccine recipients should be monitored for immediate adverse reactions according to CDC (ACIP) guidelines. (See General under Dosage and Administration.)

Vaccine recipients or their caregivers should be provided with information on, and encouraged to participate in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received a COVID-19 vaccine to identify potential adverse effects. 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 COVID-19 vaccine (Pfizer-BioNTech) report all vaccine administration errors (even if not associated with an adverse event) and serious adverse events (irrespective of attribution to vaccination) that occur following vaccination and also report all cases of multisystem inflammatory syndrome (MIS) and COVID-19 that result in hospitalization or death in vaccine recipients to VAERS. VAERS reports can be completed and submitted online at <https://vaers.hhs.gov/reportevent.html> or faxed to 877-721-0366; the words "Pfizer-BioNTech COVID-19 Vaccine EUA" should be included in the description section of the report. Information on submitting a VAERS report can be obtained by calling 800-822-7967 or emailing info@vaers.org. To the extent feasible, a copy of the VAERS form should also be provided to the manufacturer (Pfizer) at <https://www.pfizersafetyreporting.com>, 866-635-8337 (fax), or 800-438-1985 (phone).

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

Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals

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

Currently available antibody tests for SARS-CoV-2 assess IgM and/or IgG to one of two viral proteins (spike or nucleocapsid). Because COVID-19 vaccines, including the Pfizer-BioNTech COVID-19 vaccine, encode the spike protein of the virus, a positive test for spike protein IgM/IgG could indicate either prior infection or vaccination. To evaluate for evidence of prior infection in an individual with a history of COVID-19 vaccination, a test that specifically evaluates IgM/IgG to the nucleocapsid protein should be used.

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

Interpretation of Tuberculosis Tests in Vaccinated Individuals

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

If TST or IGRA is required according to administrative policies (e.g., healthcare employment, admission to long-term care facilities), such testing can be performed before or during the same visit when a COVID-19 vaccine is administered. If such tuberculosis testing cannot be done prior to or at the same time as COVID-19 vaccination, ACIP recommends that it be delayed until at least 4 weeks after completion of vaccination. If a tuberculosis testing requirement or policy cannot be modified to accept a delay in TST or IGRA testing during the COVID-19 pandemic, it should be understood that a false-negative TST or IGRA cannot be excluded and consideration should be given to repeating a negative TST or IGRA test at least 4 weeks after completion of COVID-19 vaccination. In addition, if the TST was performed as the initial test, consideration should be given to the possibility that boosting could be a factor if results of a repeat TST are positive.

ACIP states that individuals who have active tuberculosis disease or an illness that is being evaluated as active tuberculosis disease can receive COVID-19 vaccination; however, a moderate or severe acute illness usually is a precaution for vaccination

(see Concomitant Illness under Cautions). If TST or IGRA is being considered for medical diagnosis of latent tuberculosis infection (e.g., during a contact investigation after exposure to contagious tuberculosis disease), a decision to delay such testing until at least 4 weeks after completion of COVID-19 vaccination is at the discretion of the responsible medical provider and local tuberculosis program overseeing the contact investigation. If a decision is made to not delay TST or IGRA testing (e.g., in individuals at high risk for progression to tuberculosis disease) and test results are negative, ACIP states that consideration should be given to retesting at least 4 weeks after completion of COVID-19 vaccination.

Specific Populations

Pregnancy.

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

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of mRNA (30 mcg) and other ingredients included in a single human dose of the Pfizer-BioNTech COVID-19 vaccine was administered IM to female rats on 4 occasions (21 and 14 days prior to mating and on gestation days 9 and 20). No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

Observational data suggest that, while the absolute risk is low, pregnant women with COVID-19 are at increased risk of severe illness, including illness resulting in admission to an intensive care unit (ICU), mechanical ventilation, extracorporeal membrane oxygenation (ECMO), or death. Additionally, such women might be at an increased risk of adverse pregnancy outcomes, such as preterm birth.

FDA states that pregnancy is not a contraindication to use of the Pfizer-BioNTech COVID-19 vaccine, and pregnant women should discuss their options with their healthcare providers.

ACIP states that, based on current knowledge, COVID-19 vaccines are unlikely to pose a risk to pregnant women or the fetus; therefore, pregnant women may choose to be vaccinated. ACIP states that any authorized COVID-19 vaccine can be administered to pregnant women; ACIP does not state a preference for any specific COVID-19 vaccine in such women.

The American College of Obstetricians and Gynecologists (ACOG) recommends that COVID-19 vaccines should not be withheld from pregnant women. In the interest of patient autonomy, these experts recommend that pregnant women be free to make their own decision regarding COVID-19 vaccination.

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 available under an EUA; however, such a conversation is not required prior to vaccination. When making a decision, these experts recommend that the pregnant woman and her healthcare provider consider the level of COVID-19 transmission in the community, the individual's personal risk of contracting COVID-19, risks of COVID-19 to the individual and potential risks to the fetus, efficacy of the vaccine, adverse effects of the vaccine, and lack of data about use of the vaccine during pregnancy.

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

ACOG recommends 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.

Administration of other vaccines (e.g., diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed [DTaP], influenza vaccine) in pregnant women should be deferred for 14 days after COVID-19 vaccination. (See Vaccines under Drug Interactions.) ACOG states that Rh₀(D) immune globulin should not be withheld when indicated in an individual who is planning to receive or recently received a COVID-19 vaccine. (See Immune Globulins and Antibody Therapies under Drug Interactions.)

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

Females and Males of Reproductive Capacity.

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

ACIP states that 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 of the authorized COVID-19 vaccines affect future fertility.

Lactation.

Data are not available to assess whether COVID-19 vaccine (Pfizer-BioNTech) 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 Pfizer-BioNTech COVID-19 vaccine, and women who are breast-feeding should discuss their options with their healthcare providers.

ACIP states that COVID-19 vaccines are not thought to be a risk for breast-feeding women or their infants; therefore, breast-feeding women may choose to be vaccinated. ACIP states that any authorized COVID-19 vaccine can be administered to breast-feeding women; ACIP does not state a preference for any specific COVID-19 vaccine in such women.

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

Pediatric Use.

The FDA EUA permits use of COVID-19 vaccine (Pfizer-BioNTech) for the prevention of COVID-19† in adolescents 12 through 18 years of age based on safety and efficacy in this age group and in adults.

The Pfizer-BioNTech COVID-19 vaccine is not authorized for use in children younger than 12 years of age.

Geriatric Use.

Individuals 65 years of age or older have been included in clinical trials evaluating COVID-19 vaccine (Pfizer-BioNTech), and data from such individuals contribute to the overall assessment of safety and efficacy of the vaccine. At the time that FDA's safety and efficacy analyses of data from the ongoing randomized, double-blind, placebo-controlled, phase 2/3 trial were performed for the EUA, 21.4% of vaccine recipients were 65 years of age or older and 4.3% were 75 years of age or older.

■ Common Adverse Effects

Data regarding the safety of COVID-19 vaccine (Pfizer-BioNTech) are available from several clinical trials, including data for individuals enrolled in the ongoing randomized, double-blind, placebo-controlled, phase 2/3 trial (NCT04368728; C45910001; study 2). At the time that FDA's safety analysis of study 2 was performed for the EUA, a total of 37,586 study participants 16 years of age or older (18,801 in the vaccine group and 18,785 in the placebo group) had been followed for a median of 2 months after the second dose.

Local adverse effects reported following administration of the Pfizer-BioNTech COVID-19 vaccine in clinical trials include injection site pain (84.1%), swelling (10.5%), and erythema (9.5%). Most local reactions have been mild to moderate in severity; severe pain has been reported in less than 1% of vaccine recipients across all age groups. Data indicate that the median duration of adverse local effects is 2.3–2.6 days (range: 1–36 days) following administration of the second dose of the 2-dose vaccination series.

Systemic adverse effects reported following administration of the Pfizer-BioNTech COVID-19 vaccine in clinical trials include fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.1%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%). Data from the ongoing phase 2/3 trial indicate that systemic adverse effects are reported more frequently after the second dose of the 2-dose vaccination series and are reported more frequently in vaccine recipients 16–55 years of age than in those 56 years of age or older. Systemic adverse effects generally occurred within the first 1–2 days after vaccination and resolved within a few days. Use of antipyretic or pain medication within 7 days after receiving the first or second vaccine dose was reported in 27.8 or 45%, respectively, of those 18–55 years of age and in 19.9 or 37.7%, respectively, of those 56 years of age or older.

In study participants 16–55 years of age, serious adverse events have been reported in 0.4% of vaccine recipients and 0.3% of placebo recipients; in those 56 years of age or older, serious adverse events were reported in 0.8 or 0.6% of vaccine or placebo recipients, respectively.

Although immediate allergic reactions have not been reported to date in clinical trials evaluating the Pfizer-BioNTech COVID-19 vaccine, severe allergic reactions, including anaphylaxis, have been reported when mRNA COVID-19 vaccines were administered outside of clinical trials. (See Hypersensitivity Reactions under Cautions.)

Drug Interactions

■ Immune Globulins and Antibody Therapies

Individuals receiving immune globulin (e.g., immune globulin IV [IGIV], Rh₀(D) immune globulin) and antibody therapies *not* specific for SARS-CoV-2 may receive COVID-19 vaccination either concurrently with or at any interval before or after the immune globulin or antibody therapy since such products are unlikely to substantially impair immune responses to the COVID-19 vaccine. ACIP states that there is no recommended minimum interval between receipt of antibody therapies not specific for SARS-CoV-2 and COVID-19 vaccination.

SARS-CoV-2 Antibody Therapies

Data are not available regarding the safety and efficacy of administering COVID-19 vaccines to individuals who have received passive antibody therapy with investigational SARS-CoV-2-specific monoclonal antibodies (e.g., bamlanivimab,

bamlanivimab and etesevimab, casirivimab and imdevimab) or investigational COVID-19 convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of SARS-CoV-2 antibody therapies as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, ACIP recommends that COVID-19 vaccination should be deferred for at least 90 days after such therapies as a precautionary measure until additional information becomes available since this avoids potential interference of the antibody therapy with immune responses to the COVID-19 vaccine. This recommendation applies to individuals who received such antibody therapy before receiving any vaccine doses and those who received such antibody therapy after the first dose of an mRNA COVID-19 vaccine but before the second dose of the vaccine, in which case the second vaccine dose should be deferred for at least 90 days following receipt of the antibody therapy. However, COVID-19 vaccination is not contraindicated in individuals who have received passive antibody therapy within the past 90 days, and COVID-19 vaccine doses received within 90 days after receipt of passive antibody therapy do not need to be repeated.

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

■ Immunosuppressive Agents

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

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

Data are insufficient to date to inform optimal timing of COVID-19 vaccination for individuals planning to receive immunosuppressive therapies. However, based on general best practices for vaccination of immunocompromised individuals, ACIP states that COVID-19 vaccination should ideally be completed at least 2 weeks before initiation of immunosuppressive therapies. When it is not possible to administer a complete COVID-19 vaccination series (i.e., a 2-dose regimen of the Pfizer-BioNTech COVID-19 vaccine or the Moderna COVID-19 vaccine or a single dose of the Janssen COVID-19 vaccine) in advance, individuals receiving immunosuppressive therapy can still receive COVID-19 vaccination. Decisions to delay immunosuppressive therapy to complete COVID-19 vaccination should consider the individual's risks related to their underlying condition.

Based on currently available information, ACIP states that revaccination after immune competence is regained is not recommended in individuals who received a COVID-19 vaccine during chemotherapy or treatment with other immunosuppressive drugs. If an individual who received COVID-19 vaccination subsequently develops COVID-19, ACIP states that prior receipt of a COVID-19 vaccine should not affect treatment decisions, including the use of corticosteroids, or the timing of such treatment.

■ Vaccines

Data are not available to date to assess concomitant administration of the Pfizer-BioNTech COVID-19 vaccine with other vaccines.

Because of the lack of data on safety and efficacy of simultaneous administration of COVID-19 vaccines with other vaccines, ACIP states that the 2-dose vaccination series of the Pfizer-BioNTech COVID-19 vaccine should routinely be administered alone, with a minimum interval of 14 days before or after administration of any other vaccines. However, a shorter interval may be used in situations when the benefits of vaccination outweigh the potential unknown risks of concomitant administration (e.g., tetanus toxoid-containing vaccination as part of wound management; rabies vaccination for postexposure prophylaxis; measles or hepatitis A vaccination during an outbreak) or to avoid barriers or delays to COVID-19 vaccination (e.g., in long-term care facility residents or healthcare personnel who received influenza or other vaccinations prior to or at the time of admission or onboarding). If a COVID-19 vaccine is administered within 14 days of another vaccine, ACIP states that it is not necessary to repeat doses of either vaccine.

Description

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

The modRNA contained in the Pfizer-BioNTech COVID-19 vaccine encodes a membrane-anchored, full-length spike (S) glycoprotein receptor-binding domain (RBD) antigen of SARS-CoV-2 with 2 proline modifications within the central helix domain that lock the S protein in an antigenically preferred prefusion conformation. Following IM injection, the LNPs in the vaccine enable delivery of the modRNA into host cells where it is released and translated to the encoded S antigen of SARS-CoV-2. The S antigen is then incorporated into cellular membranes and elicits an immune response to provide protection against SARS-CoV-2.

Data from clinical trials in adults indicate that a 2-dose vaccination series of COVID-19 vaccine (Pfizer-BioNTech) induces SARS-CoV-2 neutralizing titers and

S1-binding IgG levels. Antibody responses are evident after the first vaccine dose and substantially boosted after the second vaccine dose, supporting the need for a 2-dose vaccination series. Follow-up data reported in vaccine recipients approximately 1 month following the second vaccine dose indicate that SARS-CoV-2 geometric mean titers (GMTs) in vaccinees are comparable to or higher than GMTs reported in convalescent serum obtained from individuals who have recovered from COVID-19. There also is some evidence from animal studies that the Pfizer-BioNTech COVID-19 vaccine can elicit strong CD4⁺ and CD8⁺ T-cell responses.

In a SARS-CoV-2 rhesus challenge model, 2 IM doses of the Pfizer-BioNTech COVID-19 vaccine or saline control were given 21 days apart followed by an intranasal or intratracheal SARS-CoV-2 challenge given 55 days after the second dose. In the vaccinated animals, S1-binding IgG was detectable by day 21 after the first vaccine dose and increased further after the second dose. Following the SARS-CoV-2 challenge, viral RNA was detected in bronchoalveolar lavage samples from control animals but was not detected in samples from the vaccinated animals. There was no clinical, radiologic, or histopathologic evidence of vaccine-elicited disease enhancement.

COVID-19 vaccine (Pfizer-BioNTech) available for use under the FDA EUA is provided as a frozen suspension concentrate in multiple-dose vials. Following thawing and dilution with 0.9% sodium chloride as directed by the manufacturer, each 0.3-mL dose of COVID-19 vaccine (Pfizer-BioNTech) contains 30 mcg of modRNA encoding the S glycoprotein of SARS-CoV-2. Each dose of the vaccine also contains LNPs composed of 4 different lipids in a defined ratio (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol) and potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose.

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

Advice to Patients

Prior to administration of COVID-19 vaccine (Pfizer-BioNTech), 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 Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 12 Years of Age or Older and given a copy of the fact sheet or directed to the manufacturer's website at <https://www.cvdvaccine.com> to obtain the fact sheet.

At the time that the first dose of the Pfizer-BioNTech COVID-19 vaccine is administered, inform the vaccine recipient or their caregiver that the vaccine is administered in a series of 2 doses given 3 weeks (21 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.

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 Pfizer-BioNTech COVID-19 vaccine, which is an investigational vaccine that has not received FDA approval, for use in individuals 12 years of age or older. 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 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 Pfizer-BioNTech 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) and systemic adverse effects (tiredness, headache, muscle pain, chills, joint pain, fever, nausea, feeling unwell, swollen lymph nodes [lymphadenopathy], nonsevere allergic reactions [rash, pruritus, hives, facial swelling]) have been reported in recipients of the Pfizer-BioNTech COVID-19 vaccine.

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., polyethylene glycol) 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 the vaccination provider if they have previously received any other COVID-19 vaccine, have any medical conditions (e.g., bleeding disorders, immunocompromising diseases), or are receiving anticoagulants or immunosuppressive therapy.

Importance of women informing clinicians if they are or plan to become pregnant or plan to breast-feed.

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

Preparations

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

COVID-19 vaccine (Pfizer-BioNTech) is not commercially available. FDA issued an emergency use authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine that permits use of the vaccine for the prevention of COVID-19† in individuals 12 years of age or older. 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 (Pfizer-BioNTech)

Parenteral

Suspension concentrate, for IM use

30 mcg (of modRNA) per 0.3-mL dose

Pfizer-BioNTech COVID-19 Vaccine, Pfizer

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

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