COVID-19 Vaccine, mRNA (Pfizer-BioNTech)

80:12 • Vaccines (AHFS primary)

Special Alerts:

Emergency Use Authorization (EUA) Changes for COVID-19 Vaccine (Pfizer BioNTech): On March 29, 2022, the EUA for the Pfizer BioNTech COVID-19 vaccine was reissued to permit use of the vaccine as a second booster dose at least 4 months after receipt of a first booster dose of any FDA-authorized or approved COVID-19 vaccine product to individuals ≥50 years of age and certain immunocompromised individuals ≥12 years of age (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise). On June 17, 2022, the EUA for Pfizer BioNTech COVID-19 vaccine was reissued to permit use of the vaccine as a 3-dose primary vaccination series in individuals 6 months to 4 years of age. For additional information, consult the EUA at https://www.fda.gov/media/150386/download and the fact sheet for healthcare providers at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine

National Alert Network (NAN) Alert Regarding Age-Related COVID-19 Vaccine Mix-ups: On December 6, 2021, the National Alert Network (NAN) issued an alert to make vaccine providers aware of reports of accidental mix-ups between the pediatric formulation of the Pfizer BioNTech COVID-19 vaccine intended for children 5–11 years of age (10 mcg/0.2 mL with an orange cap) and the adult formulation of the Pfizer BioNTech COVID-19 vaccine intended for individuals ≥12 years of age (30 mcg/0.3 mL with a purple cap). Multiple cases of such errors have been report to the ISMP National Vaccine Errors Reporting Program (ISMP VERS). In some cases, children ≥12 years of age received the formulation intended for children 5–11 years of age, resulting in underdoses; in other cases, children 5–11 years of age received the formulation intended for individuals ≥12 years of age, resulting in overdoses. Possible causes include vial and syringe mix-ups and incorrect assumption that the formulations are interchangeable. The pediatric vaccine is specifically formulated to be less concentrated to ensure accurate dose measurement; use of the adult formulation to prepare doses for children 5–11 years of age is likely to result in delivery of an inaccurate volume of vaccine to the patient. The NAN alert provides recommendations for preventing such vaccine mix-ups, which include segregate storage, proper labeling of syringes, and vaccine verification at the time of administration. For additional information, see https://www.ismp.org/sites/default/files/attachments/2021-12/NAN-20211206.pdf.

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

■ 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 used for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals ≥16 years of age. COVID-19 vaccine (Pfizer-BioNTech) received FDA approval under a biologics license application (BLA) for use as a 2-dose primary vaccination series for prevention of COVID-19 in individuals ≥16 years of age; the FDA-approved Pfizer-BioNTech COVID-19 vaccine is labeled as Comirnaty®.

Although efficacy and safety have not been established, the Pfizer-BioNTech COVID-19 vaccine is also available under an FDA emergency use authorization (EUA) as a 2-dose primary vaccination series for prevention of COVID-19 in individuals ≥5 years of age†; as an additional (third) primary dose† in certain immunocompromised individuals ≥5 years of age; as a single homologous booster dose† after completion of the primary series with the Pfizer-BioNTech COVID-19 vaccine in individuals ≥12 years of age; and as a single heterologous booster dose† in individuals ≥18 years of age who have received primary vaccination with another FDA authorized or approved COVID-19 vaccine.

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

Emergency Use Authorization

FDA issued the initial EUA for COVID-19 vaccine (Pfizer-BioNTech) on December 11, 2020 that permitted use of a 2-dose series of the vaccine to prevent COVID-19 in individuals ≥16 years of age. Since then, the EUA has been amended and reissued several times as the scope of authorization changed. The EUA for the Pfizer-BioNTech COVID-19 vaccine now permits use as:

- A 2-dose primary vaccination series in individuals ≥5 years of age.
- An additional (third) primary series dose administered at least 28 days following the second dose of the COVID-19 vaccine (Pfizer-BioNTech) in certain immunocompromised individuals ≥5 years of age (i.e., those who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise).
- A single homologous booster dose in individuals ≥12 years of age, administered at least 5 months after completion of the primary series of the COVID-19 vaccine (Pfizer-BioNTech).
- A single heterologous booster dose in individuals ≥18 years of age after completion of a primary vaccination series with another authorized or approved COVID-19 vaccine. When a heterologous vaccine product is used for the booster dose, the dosing interval is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

FDA issued the EUA for the Pfizer-BioNTech COVID-19 vaccine 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 of the vaccine outweigh the known and potential risks. The EUA for the Pfizer-BioNTech COVID-19 vaccine requires that the vaccine be administered as authorized and that vaccination providers participate and comply with terms and training required by CDC's COVID-19 vaccination program.

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 vaccine information fact sheet and ensuring that all vaccination administration errors

and all serious adverse events potentially attributable to the vaccine are reported as specified in the fact sheet.

For additional information, consult the 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 vaccine information fact sheet for recipients and caregivers (https://www.fda.gov/media/144414/download).

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). Based on results of the dose-escalation phase 1 portion of the trial that evaluated 3 different dosages of the Pfizer-BioNTech COVID-19 vaccine in healthy adults ≥18 years of age, 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 first 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. A secondary end point is the incidence of severe COVID-19 with onset at least 7 days after the second dose in participants with or without evidence of SARS-CoV-2 infection prior to 7 days after the second dose.

Primary Vaccination in Adults and Adolescents 16 Years of Age and Older.

Safety and efficacy of the Pfizer-BioNTech COVID-19 vaccine for prevention of COVID-19 in individuals ≥16 years of age as a 2-dose vaccination series were established based on review of efficacy and safety data accrued through March 13, 2021 from the ongoing phase 1/2/3 clinical trial (NCT04368728; C45910001; study 2).

The population for analysis of the protocol pre-specified primary efficacy end point included 36,621 participants ≥12 years of age (18,242 in the vaccine group and 18,379 in the placebo group) who had no evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. This included all participants ≥12 years of age who had been enrolled from July 27, 2020 and followed for the development of COVID-19 through November 14, 2020 (enrollment for those 18–55 years of age and ≥56 years of age began July 27, 2020, enrollment for those 16–17 years of age began September 16, 2020, and enrollment for those 12–15 years of age began October 15, 2020). For participants without evidence of SARS-CoV-2 infection prior to 7 days after dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after dose 2 was 95%, which met the pre-specified success criterion. There were 8 cases of COVID-19 in the vaccine group compared with 162 cases in the placebo group.

The population for the updated vaccine efficacy analysis performed for the BLA approval included participants ≥16 years of age who had been enrolled from July 27, 2020 and followed for the development of COVID-19 during blinded, placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after dose 2. A total of 12,796 participants in the vaccine group and 12,449 in the placebo group were followed for at least 4 months after dose 2 in the blinded, placebo-controlled follow-up period. Vaccine efficacy against first COVID-19 occurrence from day 7 after dose 2 in participants ≥16 years of age without evidence of infection prior to 7 days after dose 2 was 91.1% (90.5% in those 16–64 years of age and 94.5% in those ≥65 years of age).

Efficacy analyses of secondary efficacy end points supported benefit of the Pfizer-BioNTech COVID-19 vaccine in preventing *severe* COVID-19. Vaccine efficacy against first severe COVID-19 occurrence from day 7 after dose 2 in participants ≥16 years of age with or without evidence of prior SARS-CoV-2 infection who were at risk for severe COVID-19 was 95.3% (severe SARS-CoV-2 infection was confirmed in 1 of 20,540 individuals in the vaccine group and 21 of 20,629 individuals in the placebo group). Vaccine efficacy against first severe COVID-19 occurrence (based on CDC definition of severe COVID-19) in this age group from day 7 after dose 2 was 100% (no cases of severe SARS-CoV-2 infection were reported in the 20,513 individuals in the vaccine group and 31 cases were reported in the 20,593 individuals in the placebo group).

SARS-CoV-2 variants of concern identified from COVID-19 cases in this study included B.1.1.7 (Alpha; first detected in the UK) and B.1.351 (Beta; first detected in South Africa), and representation of identified variants among cases of infection in vaccine recipients compared with placebo recipients did not suggest decreased vaccine effectiveness against these variants.

Additional primary efficacy analyses among subgroups defined by sex, race, ethnicity, geography, 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.

Primary Vaccination in Adolescents 12 through 15 Years of Age.

At the time of FDA's efficacy review of data from the phase 2/3 portion of study 2 that permitted use of the Pfizer-BioNTech COVID-19 vaccine as a 2-dose primary vaccination series in adolescents 12–15 years of age† under the EUA, a descriptive efficacy analysis that included approximately 2200 adolescents 12–15 years of age had been performed and provided data for confirmed COVID-19 cases that accrued during blinded, placebo-controlled follow-up in these adolescents through March 13, 2021. Among the 1983 participants 12–15 years of age in the trial who had no evidence of existing or prior SARS-CoV-2 infection (1005 in the vaccine group and 978 in the placebo group), there were no cases of COVID-19 with onset at least 7 days after the second dose among vaccine recipients and 16 cases among placebo recipients; this corresponds to 100% vaccine efficacy. Among the 2229 participants 12–15 years of age with or without evidence of SARS CoV-2 infection prior to 7 days after the second dose (1119 in the vaccine group and 1110 in the placebo group), there were no cases of COVID-19 with onset at least 7 days after the second dose among vaccine recipients and 18 cases among placebo recipients; this corresponds to 100% vaccine efficacy.

Primary Vaccination in Children 5–11 Years of Age.

FDA authorization for use of the Pfizer-BioNTech COVID-19 vaccine as a primary vaccination series in children 5–11 years of age† was based on data from an ongoing phase 1/2/3 trial; at the time of analysis, the trial had enrolled 4695 participants, 3109 of whom received the Pfizer-BioNTech COVID-19 vaccine formulated using PBS buffer. Review of safety data did not reveal any specific safety concerns with administration of this formulation in this population. Immunogenicity analyses demonstrated that neutralizing antibody titers achieved 1 month after the second dose in individuals 5–11 years met immunobridging criteria for both geometric mean antibody titers and seroresponse rates as compared to a random sample of individuals 16–25 years of age who were enrolled in the previously referenced clinical trial. Among the 1968 participants 5–11 years of age in the trial who had no evidence of existing or prior SARS-CoV-2 infection, there were 3 cases of COVID-19 at least 7 days after the second dose among vaccine recipients and 16 cases among placebo recipients, corresponding to a vaccine efficacy of 90.7%. In participants with evidence of prior SARS-CoV-2 infection, there were no cases of COVID-19 observed in either group.

Additional Primary Dose in Immunocompromised Individuals 5 Years of Age or Older.

Efficacy and safety of an additional (third) primary series dose of the Pfizer-BioNTech COVID-19 vaccine in individuals ≥12 years of age† were evaluated in a single-arm study that included a group of 99 solid organ transplant recipients. Individuals included in the study had previously received various solid organ transplants (heart, kidney, liver, lung, pancreas) and were receiving immunosuppressive therapy, including glucocorticoids (87%), calcineurin inhibitors (79%), mycophenolic acid (63%), mammalian target of rapamycin [mTOR] inhibitors (30%), and belatacept (12%). The transplant recipients received 2 doses of Pfizer-BioNTech COVID-19 vaccine given 1 month apart, followed by a third dose of the vaccine administered approximately 2 months after the second dose. The time between transplantation and initiation of the vaccination series against COVID-19 ranged from 89–105 months. Among those who had been seronegative for anti-SARS-CoV-2 spike protein antibodies prior to the third vaccine dose, 44% were seropositive for antibodies at 4 weeks after the third dose. All 40 patients who were seropositive before the third vaccine dose were still seropositive 4 weeks after the dose (antibody titers were 36 prior to the third dose and 2676 at 1 month after the third dose). Overall, anti-SARS-CoV-2 antibodies were detected in 68% of study participants when tested at 4 weeks after the third vaccine dose. Patients who did not have an antibody response were older, had a higher degree of immunosuppression, and had a lower estimated glomerular filtration rate than patients who had an antibody response.

FDA authorization of a third primary series dose in children 5–11 years of age† who have undergone solid organ transplantation or are diagnosed with conditions that are considered to have an equivalent level of immunocompromise is based on inferred safety data from healthy children 5–11 years of age† who were vaccinated with the primary series and extrapolated vaccine efficacy data from individuals ≥12 years of age in addition to a benefit-risk assessment.

Homologous Booster Doses in Adults and Adolescents 12 Years of Age and Older.

FDA authorization of a single booster dose† of the Pfizer-BioNTech COVID-19 vaccine in adults ≥18 years of age administered at least 5 months after completion of a 2-dose primary series of the vaccine was based on a review of data from 329 adults 18–75 years of age in the ongoing phase 1/2/3 clinical trial who had no serologic or virologic evidence of prior SARS-CoV-2 infection and received a booster dose of the vaccine approximately 6 months (range: 4.8–8.8 months) after completion of the 2-

dose primary series. Effectiveness of the booster dose was based on immunobridging analyses that compared geometric mean titers (GMTs) of neutralizing antibody against the reference strain of SARS-CoV-2 (USA/WA/1/2020) at 1 month after the booster dose and 1 month after completion of the 2-dose primary series and compared seroresponse rates at these time points. A comparison of neutralizing antibody titers (based on 50% neutralizing titer [NT50]) against the reference strain at 1 month after the booster dose versus titers at 1 month after completion of the 2-dose primary series in 212 trial participants 18–55 years of age indicated that GMTs after the booster dose were approximately threefold higher than those observed after the 2-dose primary series (GMTs of 750.6 after the 2-dose primary series and 2466 after the booster dose) and met the immunobridging success criteria. The seroresponse rate (defined as achieving at least a fourfold increase in NT50 from baseline [before the primary series]) in 200 trial participants was 98% at 1 month after completion of the 2-dose primary series and 99.5% at 1 month after the booster dose and met the immunobridging success criteria. These results demonstrated that immunogenicity of the booster dose was noninferior to immunogenicity of the 2-dose primary series of the vaccine.

FDA authorization to lower the age range for the single booster dose of the Pfizer-BioNTech COVID-19 vaccine to adolescents ≥12 years (administered at least 5 months after completion of the primary series) is based on data submitted previously to support authorization of the homologous booster dose under the EUA in addition to real world data, additional publications, and a benefit-risk assessment.

Heterologous Booster Doses in Adults.

Authorization of the Pfizer-BioNTech COVID-19 vaccine as a heterologous booster dose† is based on FDA review of data from an ongoing phase 1/2 trial. At the time of review, 458 participants 19–85 years of age who had no history of a prior SARS-CoV-2 infection were evaluated; participants had completed primary vaccination with a COVID-19 vaccine (Janssen, Moderna, or Pfizer-BioNTech) and were randomized 1:1:1 to receive a booster dose of the Moderna COVID-19 vaccine, Janssen COVID-19 vaccine, or Pfizer-BioNTech COVID-19 vaccine. A booster response to the Pfizer-BioNTech COVID-19 vaccine based on neutralizing antibody titers against a pseudovirus expressing the SARS-CoV-2 spike protein with D614G mutation was demonstrated regardless of primary vaccine received.

Dosage and Administration

■ General

Pretreatment Screening

- Screen all individuals for contraindications and precautions to vaccination.

Patient Monitoring

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

Premedication and Prophylaxis

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

Dispensing and Administration Precautions

- Appropriate medications and supplies for managing immediate allergic reactions *must* be immediately available in the event that an acute anaphylactic reaction occurs following administration of COVID-19 vaccines. Healthcare personnel who are trained and qualified to recognize signs and symptoms of anaphylaxis and administer IM epinephrine should be available at vaccination sites at all times. Vaccination locations that anticipate vaccinating large numbers of people (e.g., mass vaccination clinics) should plan adequate staffing and supplies (including epinephrine) for assessment and management of anaphylaxis. (See Hypersensitivity Reactions under Cautions.)
- Syncope (vasovagal or vasodepressor reaction; fainting) may occur following administration of parenteral vaccines; such reactions usually occur within 15 minutes following vaccine administration and are reported most frequently in adolescents and young adults. Take appropriate measures to decrease the risk of injury if the vaccine recipient becomes weak or dizzy or loses consciousness (e.g., instruct the vaccine recipient to sit or lie down during and for 15 minutes after vaccination). If syncope occurs, observe the individual until symptoms resolve.

Other General Considerations

- The Pfizer-BioNTech COVID-19 vaccine is administered in a primary series of 2 doses given 3 weeks apart. At the time the first dose is administered, a vaccination record card that provides the date when the recipient needs to return for additional vaccine dose(s) should be given to the vaccine recipient or their caregiver; vaccine recipients should be counseled on the importance of completing the 2-dose primary vaccination series to optimize protection against COVID-19.
- Provide vaccine recipients or their caregiver with information on CDC's v-safe program, a voluntary smartphone-based tool that uses text messaging and web surveys to monitor for adverse effects in individuals who have received a COVID-19 vaccine. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)
- Prior to vaccination, counsel vaccine recipient or their caregiver about local and systemic adverse effects that may occur following vaccination. Unless a contraindication to vaccination exists, ACIP recommends that vaccine recipients should be encouraged to complete the 2-dose vaccination series even if they experience a local or systemic adverse effect following the first dose since this optimizes protection.
- Individuals who receive COVID-19 vaccines should follow current CDC guidance to protect themselves and others. This may include wearing a mask in certain settings with substantial or high levels of viral transmission; following application federal, state, local, tribal, or territorial laws, rules, and regulations; and following CDC travel guidance and any applicable local business or workplace guidance. (See Limitations of Vaccine Effectiveness under Cautions.)

■ Administration

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

The Pfizer-BioNTech COVID-19 vaccine is supplied in various formulations and vial presentations. There are important differences between these formulations such as method of preparation, requirement for dilution, dose volume, and storage requirements; consult the manufacturer's labeling (for the Comirnaty® product) or the FDA EUA Fact Sheets for the Pfizer-BioNTech COVID-19 vaccine authorized for use under an EUA for specific instructions on each formulation. The various formulations and vial presentations are distinguished by different color vial caps and labels.

The Comirnaty® preparation is supplied in a multi-dose vial (30 mcg/0.3 mL) in purple caps that must be diluted before use, and also in a multi-dose vial (30 mcg/0.3 mL) in gray caps that must *not* be diluted before use.

The Pfizer-BioNTech COVID-19 vaccine supplied in a multiple dose vial (10 mcg/0.2 mL) with an orange cap and label with an orange border is authorized for use in children 5–11 years of age; this formulation should *not* be used in individuals ≥12 years of age. There are 2 formulations of the Pfizer-BioNTech COVID-19 vaccine authorized for use in individuals ≥12 years of age; both formulations contain 30 mcg in each 0.3-mL dose. One formulation is supplied in a multiple dose vial with a purple cap; this formulation *must* be diluted prior to use. The other formulation does not require dilution and is supplied in a multiple dose vial with a gray cap.

The Comirnaty® Pfizer-BioNTech COVID-19 vaccine and the 2 EUA authorized formulations (purple cap and gray cap) of the Pfizer-BioNTech COVID-19 vaccine for individuals ≥12 years of age can be used interchangeably when prepared according to their respective instructions for use. *The formulations authorized for use in individuals ≥12 years of age should not be used in individuals 5–11 years of age because of the potential for vaccine administration errors, including dosing errors.*

IM Injection

Comirnaty® Vials with Purple Cap.

The COVID-19 vaccine (Pfizer-BioNTech) labeled as Comirnaty® with a purple cap must be diluted with 0.9% sodium chloride injection prior to use; the vaccine is supplied as a frozen suspension in multiple-dose vials that must be thawed prior to dilution.

The frozen vaccine may be thawed and stored for up to 1 month in a refrigerator (2–8°C) or thawed at room temperature (up to 25°C). If the room temperature method is used, allow the vials to sit at room temperature for 30 minutes. Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours. Vaccine that has been thawed must not be refrozen.

Prior to dilution, gently invert the vials 10 times; do not shake. Inspect the liquid in the vial prior to dilution; the thawed COVID-19 vaccine (Pfizer-BioNTech) suspension should appear as a white to off-white suspension, but may contain white to off-white opaque amorphous particles. Do not use the thawed vaccine if the liquid is discolored or contains other particles. Using aseptic technique, withdraw 1.8 mL of 0.9% sodium chloride injection into a 3- or 5-mL transfer syringe (21-gauge or narrower needle) and inject into the vial. To equalize vial pressure, withdraw 1.8 mL of air into the empty diluent syringe before removing the needle from the vial. After the diluent has

been added, gently invert the vial 10 times to mix; do not shake. Following dilution, the vaccine should appear as an off-white suspension and should *not* be used if it is discolored or contains particulates.

Record the date and time of dilution on the vaccine vial. The vaccine may be stored between 2–25°C, but *must* be used within 6 hours after dilution (regardless of storage temperature). Discard any unused diluted vaccine remaining in vials if not used within 6 hours after dilution.

To administer a dose of the vaccine, withdraw 0.3 mL of the diluted suspension from the vial using aseptic technique and an appropriate syringe and needle, and administer immediately. A low dead-volume syringe and needle is preferred for administration of the vaccine; however, 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 Comirnaty® Pfizer-BioNTech COVID-19 vaccine with a purple cap 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. Discard any vaccine remaining in the vial that does not constitute a full 0.3-mL dose; excess vaccine remaining in the vial must not be pooled from multiple vials to obtain a dose.

Comirnaty® Vials with Gray Cap.

The COVID-19 vaccine (Pfizer-BioNTech) labeled as Comirnaty® with a gray cap must NOT be diluted prior to use; the vaccine is supplied as a frozen suspension in multiple-dose vials that must be thawed prior to administration.

Vials may be thawed either in a refrigerator (2–8°C) or at room temperature (up to 25°C). If the room temperature method is used, allow the vials to sit at room temperature for 30 minutes. Vials may be stored at room temperature for up 12 hours prior to first use. Record the date and time of first vial puncture on the vial label. After the first puncture, the vaccine should be stored between 2–25°C; discard any unused vaccine 12 hours after first vial puncture. Vaccine that has been thawed must not be refrozen.

The thawed vaccine may contain white to off-white opaque amorphous particles. Prior to use, gently invert the vial 10 times; do not shake. After gently inverting the vial, the vaccine should appear as a white to off-white suspension with no visible particulates. Do not use the vaccine if the liquid is discolored or if particles are observed.

To administer a dose, withdraw 0.3 mL of the vaccine from the vial using aseptic technique and an appropriate syringe and needle, and administer immediately. A low dead-volume syringe and needle is preferred for administration of the vaccine; however, a standard 1-mL syringe can be used if a low dead-volume syringe is not available. Each thawed multiple dose Comirnaty® vial with a gray cap 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. Discard any vaccine remaining in the vial that does not constitute a full 0.3-mL dose; excess vaccine remaining in the vial must not be pooled from multiple vials to obtain a dose.

Multiple Dose Vials with Purple Cap Authorized for Use Under EUA.

The Pfizer-BioNTech COVID-19 vaccine supplied in a multiple dose vial with a purple cap and label is one of the formulations authorized under an FDA EUA for use in individuals ≥12 years of age; this formulation should not be used in individuals 5–11 years of age because of the potential for vaccine administration errors, including dosing errors. The multiple dose vials with a purple cap contain Pfizer-BioNTech COVID-19 vaccine formulated using phosphate buffered saline (PBS) buffer; each 0.3-mL dose of the vaccine contains 30 mcg modRNA.

The Pfizer-BioNTech COVID-19 vaccine formulation with a purple cap is shipped in thermal containers with dry ice at ultra-low temperatures and must be stored frozen at specific temperatures.

Prior to use, the vaccine must be thawed and then diluted with 0.9% sodium chloride injection *only*; other diluents (e.g., bacteriostatic 0.9% sodium chloride injection) should *not* be used.

The frozen COVID-19 vaccine (Pfizer-BioNTech) suspension concentrate may be thawed and stored for up to 1 month in a refrigerator (2–8°C) or thawed at room temperature (up to 25°C). If the room temperature method is used, allow the vials to sit at room temperature for 30 minutes. Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours. Vaccine that has been thawed *must* not be refrozen.

Thawed COVID-19 vaccine (Pfizer-BioNTech) suspension concentrate *must* equilibrate to room temperature prior to dilution. Prior to dilution, gently invert the vials 10 times; do not shake. Inspect the liquid in the vial prior to dilution; the thawed vaccine should appear as a white to off-white suspension, but may contain white to off-white opaque amorphous particles. Do not use the vaccine if the liquid is discolored or contains other particles. Using aseptic technique, withdraw 1.8 mL of 0.9% sodium chloride injection into a 3- or 5-mL transfer syringe (21-gauge or narrower needle) and inject 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, withdraw 1.8 mL of air into the empty diluent syringe before removing the needle from the vial. After the 0.9% sodium chloride diluent has been added, gently invert the vial 10 times to mix; do not shake. Following dilution, the vaccine should appear as an off-white suspension and should *not* be used if it is discolored or contains particulates.

Record the date and time of dilution 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.

To administer a dose, withdraw 0.3 mL of the vaccine from the vial using aseptic technique and an appropriate syringe and needle, and administer immediately. A low dead-volume syringe and needle is preferred for administration of the vaccine; however, a standard 1-mL syringe can be used if a low dead-volume syringe is not available. Each diluted Pfizer-BioNTech COVID-19 vaccine vial with a purple cap 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. Discard any vaccine remaining in the vial that does not constitute a full 0.3-mL dose; excess vaccine remaining in the vial must not be pooled from multiple vials to obtain a dose.

Multiple Dose Vials with Gray Cap Authorized for Use Under EUA.

The Pfizer-BioNTech COVID-19 vaccine supplied in a multiple dose vial with a gray cap and label is one of the formulations authorized for use under an FDA EUA for individuals ≥12 years of age; this formulation should not be used in individuals 5–11 years of age because of the potential for vaccine administration errors, including dosing errors. The multiple dose vials with a gray cap contain Pfizer-BioNTech COVID-19 vaccine formulated using tromethamine (Tris) buffer; each 0.3-mL dose of the vaccine contains 30 mcg modRNA. The vaccine formulation with a gray cap is supplied as a frozen suspension that must *not* be diluted prior to use. The vials may arrive frozen in thermal containers with dry ice; once received the frozen vials may be immediately transferred to the refrigerator and thawed and stored for up to 10 weeks, or stored in an ultra-low temperature freezer. If stored in the refrigerator, the 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. Alternatively, the Pfizer-BioNTech COVID-19 vaccine vials with gray caps and labels may arrive at 2–8°C; in this case, the vials should be stored at 2–8°C after receipt. Regardless of storage condition, the vaccine should not be used after 9 months from the date of manufacture printed on the vial and cartons.

Prior to use, the frozen Pfizer-BioNTech COVID-19 multiple dose vials with gray caps must be thawed. Vials may be thawed either in a refrigerator (2–8°C) or at room temperature (up to 25°C). If the room temperature method is used, allow the vials to sit at room temperature for 30 minutes. Vials may be stored at room temperature for up 12 hours prior to first puncture. Record the date of time of first vial puncture on the vial label. After the first puncture, the vaccine should be stored between 2–25°C; discard any unused vaccine 12 hours after first vial puncture. Vaccine that has been thawed must not be refrozen.

The thawed Pfizer-BioNTech COVID-19 vaccine may contain white to off-white opaque amorphous particles. Prior to use, gently invert the vials 10 times; do not shake. After gently inverting the vial, the vaccine should appear as a white to off-white suspension with no visible particulates. Do not use the vaccine if the liquid is discolored or if particles are observed.

To administer a dose, withdraw 0.3 mL of the vaccine from the vial using aseptic technique and an appropriate syringe and needle, and administer immediately. A low dead-volume syringe and needle is preferred for administration of the vaccine; however, a standard 1-mL syringe can be used if a low dead-volume syringe is not available. Each multiple dose vial 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. Discard any vaccine remaining in the vial that does not constitute a full 0.3-mL dose; excess vaccine remaining in the vial must not be pooled from multiple vials to obtain a dose.

Multiple Dose Vials with Orange Cap Authorized for Use Under EUA.

The Pfizer-BioNTech COVID-19 vaccine formulation authorized for use in children 5–11 years of age is supplied in a multiple dose vial with an orange cap and label and uses Tris buffer; each 0.2-mL dose contains 10 mcg modRNA. The vaccine formulation with an orange cap is supplied as a frozen suspension concentrate that must be diluted before use. The vials may arrive frozen in thermal containers with dry ice at ultra-low temperatures; once received, the frozen vials may be transferred immediately to the refrigerator and stored for up to 10 weeks, or stored in an ultra-low temperature freezer. If stored in the refrigerator, the 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. Alternatively, the Pfizer-BioNTech COVID-19 vaccine vials with orange caps and labels may arrive at 2–8°C; in this case, the vials should be stored at 2–8°C after receipt. Regardless of storage condition, the vaccine should not be used after 9 months from the date of manufacture printed on the vial and cartons.

Prior to use, the frozen Pfizer-BioNTech COVID-19 multiple dose vials with orange caps must be thawed and diluted with 0.9% sodium chloride injection only; do not use bacteriostatic 0.9% sodium chloride injection or any other diluent. Vials may be thawed either in a refrigerator (2–8°C) or at room temperature (up to 25°C); if the room temperature method is used, allow the vials to sit at room temperature for 30 minutes. Vials of vaccine may be stored at room temperature for up 12 hours prior to use. The thawed suspension concentrate should appear as a white to off-white suspension, but may contain white to off-white opaque amorphous particles; do not use the vaccine if it is discolored or contains other particles. Vaccine that has been thawed must not be refrozen.

To dilute the thawed vaccine suspension concentrate, gently invert the vial 10 times; do not shake. Using aseptic technique, withdraw 1.3 mL of 0.9% sodium chloride injection into a 3- or 5-mL transfer syringe (21-gauge or narrower needle) and add to the thawed vaccine vial. To equalize vial pressure, 1.3 mL of air should be withdrawn into the empty diluent syringe before removing the needle from the vial. After the diluent has been added to the vaccine, gently invert the vial 10 times to mix; do not shake. Following dilution, the vaccine should appear as an off-white suspension; do not use if the solution is discolored or contains particulates. Diluted Pfizer-BioNTech COVID-19 vaccine in multiple dose vials with orange caps may be stored at 2–25°C, but must be used within 12 hours after dilution (regardless of storage temperature). Discard any unused vaccine remaining in vials if not used within 12 hours after dilution.

Prior to vaccine administration, verify that the vial of Pfizer-BioNTech COVID-19 vaccine has an orange plastic cap and a label with an orange border that states "Age 5 y to <12 y." To administer a dose, withdraw 0.2 mL of the vaccine from the vial using aseptic technique and an appropriate syringe and needle, and administer immediately. A low dead-volume syringe and needle is preferred for administration of the vaccine; however, a standard 1-mL syringe can be used if a low dead-volume syringe is not available. Each thawed and diluted Pfizer-BioNTech COVID-19 multiple dose vial with an orange cap provides ten 0.2-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 10 doses from the vial. Irrespective of the type of syringe and needle used, each dose must contain 0.2 mL of vaccine. Discard any vaccine remaining in the vial that does not constitute a full 0.2-mL dose; excess vaccine remaining in the vial must not be pooled from multiple vials to obtain a dose.

■ Dosage

Pfizer-BioNTech COVID-19 vaccine is available in various formulations and vial presentations. Ensure the correct age-appropriate formulation is selected for administration. Pfizer-BioNTech COVID-19 vaccine (Comirnaty®) and the 2 EUA authorized 30 mcg/0.3 mL formulations should not be used for individuals 5–11 years of age in order to avoid vaccine administration errors, including dosing errors.

A 2-dose regimen of Pfizer-BioNTech COVID-19 vaccine is considered a complete primary vaccination series. Individuals should generally not receive more than one complete 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).

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

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 primary vaccination series.

Pfizer-BioNTech COVID-19 vaccine (Comirnaty®) and Pfizer-BioNTech COVID-19 vaccine 30 mcg formulations (purple and gray cap and label) without a trade name can be used interchangeably to provide the vaccination series without any safety or efficacy concerns when prepared based on their respective instructions.

Doses for the primary vaccination series and the additional primary dose, if indicated, should be completed with the same vaccine product.

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 product. ACIP states that in *exceptional* situations when the mRNA COVID-19 vaccine used for the first dose cannot be determined or is not available, any available mRNA COVID-19 vaccine approved or authorized by FDA may be administered with a minimum interval of 28 days between doses to complete the mRNA COVID-19 vaccination series. If 2 doses of *different* mRNA COVID-19 vaccines are administered in such situations (or inadvertently), the primary series is considered complete.

Additionally, ACIP states that, in limited, *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the vaccination series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), a single dose of the Janssen COVID-19 vaccine administered at least 28 days after the first dose of mRNA COVID-19 vaccine may be considered. An individual who receives a dose of an mRNA COVID-19 vaccine followed by a single dose of the Janssen COVID-19 vaccine under such exceptional circumstances should be considered to have received complete single-dose vaccination with Janssen COVID-19 vaccine (not a mixed vaccination series) and is considered fully vaccinated against COVID-19 if at least 2 weeks have elapsed since the single dose of Janssen COVID-19 vaccine.

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

See Table 1 for recommended doses and dosing intervals for the Pfizer-BioNTech COVID-19 Vaccine.

Table 1. Pfizer-BioNTech COVID-19 Vaccine Primary Series, Additional Primary Dose, and Booster Dose Recommendations

	PRIMARY SERIES	PRIMARY SERIES	BOOSTER DOSE
Indicated population	All individuals ≥12 years of age	Individuals 5–11 years of age	All individuals ≥12 years of age
Vial cap and label	Purple or gray	Orange	Purple or gray
Dose	30 mcg	10 mcg	30 mcg
Injection volume	0.3 mL	0.2 mL	0.3 mL
Recommended doses and interval	2 doses, administered 21 days apart Additional (third) primary dose of 0.3 mL recommended ≥28 days after completion of primary series in immunocompromised individuals	2 doses, administered 21 days apart Additional (third) primary dose of 0.2 mL recommended ≥28 days after completion of primary series in immunocompromised individuals	1 dose, administered ≥5 months after completion of primary series (including additional dose)

Adult Dosage

Primary Vaccination Series.

Adults should receive two 0.3-mL doses of COVID-19 vaccine (Pfizer-BioNTech) administered 3 weeks apart.

Additional Primary Dose in Immunocompromised Adults.

The FDA EUA permits administration of an additional (third) primary dose† of 0.3 mL of the Pfizer-BioNTech COVID-19 vaccine at least 28 days after the second dose in adults who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise. (See Individuals with Altered Immunocompetence under Cautions.)

Booster Dose.

The FDA EUA permits administration of a single homologous booster dose† of 0.3 mL of the Pfizer-BioNTech COVID-19 vaccine at least 5 months after completion of the primary vaccine series in individuals ≥18 years of age.

The FDA EUA permits administration of a single heterologous booster dose† of 0.3 mL of the Pfizer-BioNTech COVID-19 vaccine following completion of primary vaccination with another authorized or approved COVID-19 vaccine. When a heterologous vaccine product is used for the booster dose, the dosing interval should follow the interval recommended by the vaccine product used in the primary series. For example, those who received a single dose Janssen primary series can receive an mRNA COVID-19 vaccine booster dose at least 2 months (8 weeks) after completing their Janssen primary series.

Pediatric Dosage

Primary Vaccination Series.

Adolescents 16–17 years of age: for primary vaccination, administer two 0.3-mL doses of the Pfizer-BioNTech COVID-19 vaccine 30 mcg/0.3 mL formulation 3 weeks apart.

Adolescents 12–15 years of age†; for primary vaccination in this age group, the FDA EUA authorizes two 0.3-mL doses of the Pfizer-BioNTech COVID-19 vaccine 30 mcg/0.3 mL formulation administered 3 weeks apart.

Children 5–11 years of age†; for primary vaccination in this age group, the FDA EUA authorizes two 0.2-mL doses of the Pfizer-BioNTech COVID-19 vaccine 10 mcg/0.2 mL (orange cap) formulation administered 3 weeks apart.

Additional Primary Dose in Immunocompromised Individuals.

The FDA EUA permits administration of an additional (third) primary dose† of the Pfizer-BioNTech COVID-19 vaccine at least 28 days after the second dose in individuals ≥5 years of age who are solid organ transplant recipients or diagnosed

with conditions considered to have an equivalent level of immunocompromise. The additional primary dose is 0.2 mL (using the 10 mcg/0.2 mL formulation [orange cap]) in children 5–11 years of age or 0.3 mL (using the 30 mcg/0.3 mL formulation [purple or gray cap]) in adolescents ≥12 years of age. (See Individuals with Altered Immunocompetence under Cautions.)

Booster Dose.

The FDA EUA permits administration of a single homologous booster dose† of 0.3 mL of the Pfizer-BioNTech COVID-19 vaccine at least 5 months after completion of the primary vaccine series in adolescents ≥12 years of age.

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]).
- 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 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).

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 Pfizer-BioNTech vaccine trial to evaluate for constellations of unsolicited adverse events using preferred terms that could represent various diseases and conditions including, but 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 the mRNA COVID-19 vaccines. ACIP states that consideration can be given to using an alternative COVID-19 vaccine (Janssen COVID-19 vaccine) in such individuals provided certain measures are taken. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine.

Known (diagnosed) allergy to a component of the vaccine (e.g., PEG): ACIP considers this a **contraindication** to vaccination with the mRNA COVID-19 vaccines. ACIP states that consideration can be given to using an alternative COVID-19 vaccine (Janssen COVID-19 vaccine) in such individuals. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine.

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 or more of which is a component of a COVID-19 vaccine), but it is not known which component elicited the reaction: ACIP considers this a **precaution**, but not a contraindication, to the COVID-19 vaccine.

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

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

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

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

individuals should be observed for 15 minutes. In addition, vaccine recipients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site.

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

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

Lymphadenopathy

Lymphadenopathy 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. Some experts suggest that consideration should be given to scheduling routine screening mammography or ultrasound prior to the first dose of an mRNA COVID-19 vaccine or 4–6 weeks following the second dose of the vaccine, if possible, and if this would not unduly delay appropriate care.

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

Myocarditis and Pericarditis

There have been rare reports of acute myocarditis or pericarditis in recipients of mRNA COVID-19 vaccines (Pfizer-BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine) during post-authorization and post-marketing surveillance; the reports suggest an increased risk of myocarditis and pericarditis following vaccination, particularly within 7 days following the second dose. Symptom onset typically occurs within 2–7 days (range: 0–40 days) after receipt of a dose of an mRNA COVID-19 vaccine, and such cases have been reported more frequently after the second vaccine dose than the first dose. Available observational data have suggested an increased risk of myocarditis and pericarditis with the Moderna COVID-19 vaccine as compared to other authorized or approved COVID-19 vaccines, including the Pfizer-BioNTech COVID-19 vaccine; however, in the 12–17 age group, no comparative data exists because the Pfizer-BioNTech vaccine is the only authorized COVID-19 vaccine.

Data to date indicate that myocarditis and pericarditis following vaccination with an mRNA COVID-19 vaccine have predominantly occurred in male adolescents and young adults (range: 12–29 years of age). The observed risk of myocarditis and pericarditis is higher among males younger than 40 years of age than among females and older males and is highest in males 12–17 years of age. Although most patients were hospitalized for short periods and some required intensive care support, available data from short-term follow-up suggest that the majority of these individuals responded to conservative treatment with rapid improvement or resolution of symptoms. Additional data are needed regarding the potential for long-term sequelae.

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

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

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

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

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

Thrombocytopenia

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

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

Concomitant Illness

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

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

Individuals with Current SARS-CoV-2 Infection.

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

interval between SARS-CoV-2 infection and COVID-19 vaccination, evidence to date suggests that the risk of reinfection is low in the period after initial infection, but may increase with time due to waning immunity.

Individuals with Prior SARS-CoV-2 Infection.

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

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

Individuals with a History of Multisystem Inflammatory Syndrome.

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

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

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

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

Individuals with Underlying Medical Conditions

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

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

Individuals with Altered Immunocompetence.

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

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

Data from small studies have demonstrated that administration of an additional primary dose of mRNA COVID-19 vaccine after the initial 2-dose vaccination series may enhance immune responses to the vaccine in some immunocompromised individuals. Results of a study evaluating the safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine in solid organ transplant recipients indicate that the third dose is only moderately effective in increasing potentially protective antibody titers in such patients.

Data indicate that the frequencies of solicited local and systemic adverse effects following administration of the Pfizer-BioNTech COVID-19 vaccine in individuals with chronic, stable HIV infection (defined as viral load less than 50 copies/mL and $CD4^+$ T-cell counts exceeding 200 cells/mm^3 within 6 months before enrollment and on stable antiretroviral therapy for at least 6 months) are similar to or lower than those observed overall in individuals 16 years of age or older who received the vaccine in clinical trials.

The FDA EUA for the Pfizer-BioNTech COVID-19 vaccine permits administration of an additional (third) primary dose of the vaccine at least 28 days after completion of the initial 2-dose vaccination series in individuals ≥5 years of age who are solid organ transplant recipients or diagnosed with conditions considered to have an equivalent level of immunocompromise.

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

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

Individuals with Autoimmune Conditions.

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

Individuals with Liver Disease.

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

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

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

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

ACIP states that individuals with a history of GBS may receive any COVID-19 vaccine approved or authorized by FDA, unless they have a contraindication to the vaccine.

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

Individuals with a History of Bell's Palsy.

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

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 and 2 cases in participants who received placebo. 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 vaccine dose in the other individuals. FDA stated that these 4 cases in the vaccine group do not represent a frequency greater than that expected in the general population, and currently available information is insufficient to determine a causal relationship to the vaccine.

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

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

Individuals with Increased Bleeding Risk.

Individuals who have bleeding disorders or are receiving anticoagulant therapy 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.

Individuals Vaccinated Outside the US

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

Limitations of Vaccine Effectiveness

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

The Pfizer-BioNTech COVID-19 vaccine is administered in a primary vaccination series of 2 doses given 3 weeks apart (see Dosage under Dosage and Administration). At the time of the EUA issuance, data from the ongoing randomized, 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.

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

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

Based on the unknown duration of vaccine-induced protection and the unknown extent of protection against emerging SARS-CoV-2 variants, individuals who receive COVID-19 vaccination and are considered fully vaccinated (see Dosage under Dosage and Administration) and those who have received a third primary dose or a booster dose of the vaccine should be counseled to continue to follow current CDC interim guidance for fully vaccinated individuals to protect themselves and others. This may include wearing a mask in certain settings with substantial or high levels of viral transmission; following federal, state, local, tribal, or territorial laws, rules, and regulations; and following CDC travel guidance and any applicable local business or workplace guidance. These recommendations (available at the CDC website at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html) should be consulted for information on precautionary measures that fully vaccinated individuals should take in various social situations and/or following exposure to someone with suspected or confirmed COVID-19.

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

If COVID-19 breakthrough infection occurs in an individual who has received one or more doses of a COVID-19 vaccine, COVID-19 treatment guidelines, such as those from the National Institutes of Health (https://www.covid19treatmentguidelines.nih.gov/) or Infectious Diseases Society of America (https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/), should be consulted for treatment decisions, including use of SARS-CoV-2-specific monoclonal antibodies, convalescent plasma, antivirals, or corticosteroids. For purposes of surveillance, breakthrough infections in fully vaccinated individuals are defined as detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected at least 14 days after completion of a primary vaccination series. Breakthrough infections in fully vaccinated individuals that result in hospitalization or death should be reported to VAERS. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Duration of Immunity

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

Improper Storage and Handling

Improper storage or handling of vaccines may reduce or destroy vaccine potency resulting in inadequate or no immune response in vaccine recipients. 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.

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 for uses authorized under the FDA EUA. 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.

Vaccine recipients or their caregivers should be provided with information on, and encouraged to participate in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received

a COVID-19 vaccine to identify potential adverse effects. Information on v-safe is available at https://www.cdc.gov/vsafe.

It is mandatory that vaccination providers administering COVID-19 vaccine (Pfizer-BioNTech) report all vaccine administration errors (even if not associated with an adverse event) and all 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 administering the Pfizer-BioNTech COVID-19 vaccine under the EUA that is available at the FDA website (https://www.fda.gov/media/144413/download) and the manufacturer's website (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.

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

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

Interpretation of Tuberculosis Tests in Vaccinated Individuals

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

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

Specific Populations

Pregnancy.

Data are insufficient to date regarding use of COVID-19 vaccine (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.

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

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

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

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

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

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

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

ACOG states that Rh_0(D) immune globulin should not be withheld when indicated in an individual who is planning to receive or recently received a COVID-19 vaccine. (See Immune Globulins and Antibody Therapies under Drug Interactions.)

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

A pregnancy exposure registry has been established to monitor pregnancy outcomes in women who receive COVID-19 vaccines during pregnancy, and such women are encouraged to enroll in the registry at https://mothertobaby.org/ongoing-study/covid19-vaccines/ Individuals who receive a COVID-19 vaccine during pregnancy and those who become pregnant within 30 days after receiving a COVID-19 vaccine also should be encouraged to participate in CDC's v-safe program. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

Females and Males of Reproductive Capacity.

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

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

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

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

Lactation.

It is not known whether COVID-19 vaccine (Pfizer-BioNTech) is distributed into milk. Data are not available to assess whether the vaccine administered to a woman who is breast-feeding has any effects on the breast-fed infant or milk production.

The benefits of breast-feeding and the importance of the Pfizer-BioNTech COVID-19 vaccine to the woman should be considered along with any potential adverse effects on the breast-fed child from the vaccine or from the underlying maternal condition (i.e., susceptibility to SARS-CoV-2 infection).

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 the benefits and risks of vaccination with their healthcare providers.

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

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

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

Pediatric Use.

Safety and effectiveness of COVID-19 vaccine (Pfizer-BioNTech) for prevention of COVID-19 in individuals 16 through 17 years of age is based on safety and effectiveness data in this age group and in adults. Safety and effectiveness of the vaccine have not been fully established in individuals younger than 16 years of age.

The FDA EUA permits use of the COVID-19 vaccine (Pfizer-BioNTech) for the prevention of COVID-19 in adolescents ≥12 years of age† based on safety and efficacy in adolescents and in adults. The FDA EUA further permits use of the COVID-19 vaccine (Pfizer-BioNTech) 10 mcg/0.2 mL formulation for prevention of COVID-19 in children 5–11 years of age† based on safety and effectiveness in this age group in addition to data from the adolescent and adult populations.

The Pfizer-BioNTech COVID-19 vaccine is *not* authorized for use as a homologous booster dose in individuals <12 years of age and is not authorized for use as a heterologous booster dose in individuals <18 years of age.

Geriatric Use.

Individuals ≥65 years of age 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.

Data from the ongoing phase 1/2/3 clinical trial indicate that, as of March 13, 2021, 20.7% of the total number of individuals who received a 2-dose primary series of the vaccine were ≥65 years of age and 4.2% were ≥75 years of age. No overall differences in safety or effectiveness were observed between those ≥65 years of age and younger recipients of the vaccine.

Safety of a single booster dose† of the Pfizer-BioNTech COVID-19 vaccine in individuals ≥65 years of age is based on safety data for 12 individuals 65–85 years of age and 306 individuals 18–55 years of age who received a booster dose of the vaccine in the ongoing phase 1/2/3 clinical trial and effectiveness in individuals ≥65 years of age is based on data for 306 individuals 18–55 years of age who received a booster dose of the vaccine in the trial.

■ Common Adverse Effects

Data regarding the safety of COVID-19 vaccine (Pfizer-BioNTech) in individuals ≥16 years of age and those 12–15 years of age† 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). Data regarding the safety of COVID-19 vaccine (Pfizer-BioNTech) in children 5–11 years of age† are available from an ongoing, placebo-controlled, phase 2/3 trial (study 3).

Local adverse effects (≥10%) in adults and adolescents 16 years of age or older following administration of any dose of the Pfizer-BioNTech COVID-19 vaccine in clinical trials: Injection site pain (88.6%) and swelling (10.6%) in those 16 through 55 years of age and injection site pain (78.2%), erythema (10.4%), and swelling (11.8%) in those ≥56 years of age. Most local reactions were mild to moderate in severity; severe pain was reported in up to 1.5% of vaccine recipients. The mean duration of adverse local effects following administration of the second dose of the 2-dose vaccination series was 2.1–3 days (range: 1–70 days for injection site pain, 1–34 days for erythema, and 1–34 days for swelling).

Systemic adverse effects (≥10%) in adults and adolescents 16 years of age or older following administration of any dose of the Pfizer-BioNTech COVID-19 vaccine in clinical trials: Fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), and fever (17.8%) in those 16 through 55 years of age and fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), and fever (11.5%) in those 56 years of age or older. 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 primary 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 45.2%, respectively, of those 18–55 years of age and in 19 or 37%, respectively, of those 56 years of age or older. In study participants 16–55 years of age, serious adverse events have been reported in 0.8% of vaccine recipients and 0.9% of placebo recipients; in those 56 years of age or older, serious adverse events were reported in 1.8 or 1.7% of vaccine or placebo recipients, respectively.

Adolescents 12–15 years of age† who received a 2-dose primary series: Local adverse effects reported in a clinical trial were injection site pain (90.5%), swelling (9.2%), and erythema (8.6%); mean duration of pain at the injection site in these adolescents was 2.4 days (range: 1–10 days) after the first dose. Systemic adverse effects were fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), lymphadenopathy (0.8%), and nausea (0.4%). Use of antipyretic or pain medication within 7 days after receiving the first or second vaccine dose was reported in 36.6 or 50.8%, respectively, of these adolescents. Serious adverse events were reported in 0.4% of vaccine recipients and 0.1% of placebo recipients.

The additional (third) primary dose† in solid organ transplant recipients: Adverse event profile following a third dose in transplant (heart, kidney, liver, lung, pancreas) recipients was similar to that following the second dose; no grade 3 or 4 adverse events were reported during 1 month of follow-up after the third dose.

Single booster dose† administered approximately 6 months after 2-dose primary series of Pfizer-BioNTech COVID-19 vaccine in adults 18–55 years of age: Local adverse effects were pain (83%), erythema (5.9%), and swelling (9%); mean duration was 2.6 days (range: 1–8 days) for pain at the injection site, 2.2 days (range: 1–15 days) for erythema, and 2.2 days (range: 1–8 days) for swelling. Systemic adverse effects were fatigue (63.7%), headache (48.4%), muscle pain (39.1%), chills (29.1%), joint pain (25.3%), fever (8.7%), diarrhea (8.7%), and vomiting (1.7%). Use of antipyretic or pain medication within 7 days after receiving the booster dose was reported in 46.7% of these adults. No serious adverse events were reported through 30 days after the booster dose.

Children 5–11 years of age† who received a 2-dose primary series: Local adverse effects reported in a clinical trial were pain at the injection site (84.3%), injection site redness (26.4%), injection site swelling (20.4%); mean duration of pain at the injection site after second dose was 2.3 days in children. Systemic adverse effects were fatigue (51.7%), headache (38.2%), muscle pain (17.5%), chills (12.4%), fever (8.3%), joint pain (7.6%), lymphadenopathy (0.9%), nausea (0.4%), rash (0.3%), malaise (0.1%), and decreased appetite (0.1%). Use of antipyretic or pain medication within 7 days after receiving the first or second vaccine dose was reported in 14.4 or 19.7%, respectively, of these children. No serious adverse events were reported that were considered related to vaccination.

Other adverse effects reported during post-authorization and post-marketing surveillance include cardiac effects (myocarditis, pericarditis), GI effects (diarrhea, vomiting), hypersensitivity reactions (anaphylaxis, rash, pruritus, urticaria, angioedema), extremity pain (arm), and syncope.

Drug Interactions

■ Antithrombotic Agents

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

■ Antiviral Agents

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

■ Immune Globulins and Antibody Therapies

Individuals receiving immune globulin (e.g., immune globulin IV [IGIV], $Rh_0(D)$ immune globulin) and antibody therapies *not* specific for SARS-CoV-2 may receive COVID-19 vaccination either concurrently with or at any interval before or after the immune globulin or antibody therapy since such products are unlikely to substantially impair immune responses to the COVID-19 vaccine. ACIP states that there is no recommended minimum interval between receipt of antibody therapies not specific for SARS-CoV-2 and COVID-19 vaccination.

SARS-CoV-2 Antibody Therapies

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

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

■ Immunosuppressive Agents

Individuals receiving immunosuppressive therapy (e.g., cancer chemotherapy, corticosteroids, radiation) may have diminished or suboptimal antibody responses to vaccines, including the 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 or resumption of immunosuppressive therapies whenever possible. The level of immunocompromise and timing of vaccination with the primary series, additional primary dose, booster dose, and revaccination is best determined with the individual's clinical team.

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

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

■ Vaccines

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

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

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

Description

COVID-19 vaccine (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.

Immunogenicity of the Pfizer-BioNTech COVID-19 vaccine in adolescents 12–15 years of age was evaluated based on data from a randomly selected subset (immunogenicity subset) of participants enrolled in an ongoing clinical trial of the vaccine (NCT04368728; C45910001; study 2) who had no serologic or virologic evidence of past SARS-COV-2 infection up to 1 month after the second dose of the vaccine. Analysis of SARS-CoV-2 GMT for 50% neutralizing titer 1 month after the second vaccine dose demonstrated that immune responses in adolescents 12–15 years of age were noninferior (within 1.5-fold) compared with immune responses in those 16–25 years of age. The SARS-CoV-2 GMT was 1239.5 in those 12–15 years of age compared with 705.1 in those 16–25 years of age. Analysis of a subset of participants in an ongoing phase 1/2/3 trial of individuals 5–11 years of age similarly demonstrated that neutralizing antibody titers achieved after the second dose in individuals 5–11 years of age met immunobridging criteria for both geometric mean antibody titers and seroresponse rates as compared to a random sample of individuals 16–25 years of age.

There are 2 dosage formulations of COVID-19 vaccine (Pfizer-BioNTech) authorized for use, which are provided in 3 different multiple-dose vials, which are distinguished by different colored vial caps and labels. COVID-19 vaccine (Pfizer-BioNTech) labeled as Comirnaty® is additionally available in multiple-dose vials in 2 formulations and vial presentations (distinguished by a purple cap or gray cap).

For multiple dose vials with purple caps and labels, each 0.3-mL dose 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.

For multiple dose vials with gray caps and labels, each 0.3-mL dose 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 tromethamine, tromethamine hydrochloride, and sucrose.

For multiple dose vials with orange caps and labels, each 0.2-mL dose contains 10 mcg of modRNA encoding the S glycoprotein of SARS-CoV-2.R70 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 tromethamine, tromethamine hydrochloride, and sucrose.

All of the Pfizer-BioNTech COVID-19 vaccine formulations do not contain preservatives; vial stoppers are not made with natural rubber latex.

Advice to Patients

- Prior to administration of COVID-19 vaccine (Pfizer-BioNTech) labeled as Comirnaty® or without a trade name, must provide vaccine recipient or their caregiver with information consistent with the vaccine information fact sheet for recipients and caregivers of the Pfizer-BioNTech COVID-19 vaccine and either give them a copy of the fact sheet or direct them to the manufacturer's website at https://www.cvdvaccine.com to obtain the fact sheet.
- Inform vaccine recipients or their caregivers that the Pfizer-BioNTech COVID-19 vaccine is approved by FDA for use as a 2-dose primary series in individuals ≥16 years of age and is authorized by FDA under an EUA for use as a 2-dose primary series in individuals ≥5 years of age†, an additional (third) primary dose† in certain immunocompromised individuals ≥5 years of age, a homologous booster dose† in individuals ≥12 years of age, and a heterologous booster dose† in individuals ≥18 years of age. Advise them that clinical trials have shown that a 2-dose series of the vaccine can prevent COVID-19; however, the duration of protection following vaccination is unknown and the vaccine may not protect everyone who receives it.
- At the time that the first dose of the Pfizer-BioNTech COVID-19 vaccine is administered, inform vaccine recipient or their caregiver that the vaccine is administered in a series of 2 primary doses given 3 weeks apart and advise them of the importance of receiving the second dose of the 2-dose vaccination series to optimize protection against COVID-19. Provide vaccine recipient or their caregiver with a vaccination card that provides the date when recipient needs to return for additional vaccine dose(s) and inform them of the importance of bringing the card when they return for the next dose.
- Inform individuals who are immunocompromised that they may receive a third primary dose of the Pfizer-BioNTech COVID-19 vaccine at least 4 weeks after the second dose. Advise such individuals that the third dose may still not provide full immunity to COVID-19 and they should continue to follow preventative measures (e.g., wearing a mask).
- Advise vaccine recipients to report any adverse reactions that occur following vaccination to VAERS at 800-822-7967 or https://www.vaers.hhs.gov/.
- Provide 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 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], decreased appetite, diarrhea, vomiting, fainting in association with injection of the vaccine) have been reported in recipients of the vaccine.
- Inform vaccine recipients or their caregivers that myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have been reported rarely in some recipients of the Pfizer-BioNTech COVID-19 vaccine with symptom onset usually within a few days after the second vaccine dose. Importance of immediately seeking medical attention if chest pain, shortness of breath, or fast-beating, fluttering, or pounding heart occurs.
- Importance of vaccine recipient informing 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 and may include difficulty breathing, swelling of the face and throat, fast heartbeat, bad rash all over the body, and dizziness and weakness.
- Importance of vaccine recipient informing the vaccination provider if they have had a severe allergic reaction to any ingredient in the vaccine (e.g., PEG) or if they had a severe allergic reaction after receiving first dose of the 2-dose vaccination series; importance of such individuals *not* receiving the vaccine.
- Importance of vaccine recipient informing the vaccination provider if they previously received any other COVID-19 vaccine, have ever fainted in association with an injection, have any medical conditions (e.g., bleeding disorders, myocarditis or pericarditis, immunocompromising diseases), or are receiving anticoagulants or immunosuppressive therapy.
- Importance of women informing clinicians if they are or plan to become pregnant or plan to breast-feed. Encourage women who receive a COVID-19 vaccine around the time of conception or during pregnancy to enroll in the pregnancy registry at https://mothertobaby.org/ongoing-study/covid19-vaccines/. Also encourage those who receive a COVID-19 vaccine during pregnancy or become pregnant within 30 days after receiving a COVID-19 vaccine to participate in CDC's v-safe program.

Overview® (see Users Guide). It is *essential* that manufacturer's labeling and the Emergency Use Authorization (EUA) prescribing information contained in the Fact Sheet for Health Care Providers (https://www.fda.gov/media/144413/download) be consulted for more detailed information on dosage and administration, cautions, precautions, and contraindications for COVID-19 vaccine (Pfizer-BioNTech). The EUA Fact Sheet for Health Care Providers also should be consulted for complete information on the conditions for use of the drug 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.

Allocation of Pfizer-BioNTech COVID-19 vaccine (with or without a trade name) is being directed by the US government. The vaccine will be supplied either directly from the manufacturer or through authorized US distributor(s) 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

10 mcg (of modRNA) per 0.2-mL dose	
	Pfizer-BioNTech COVID-19 Vaccine (formulated with Tris buffer; available in multiple dose vials with orange caps and labels), Pfizer
30 mcg (of modRNA) per 0.3-mL dose	
	Comirnaty® (available in multiple dose vials with purple caps and labels or gray caps and labels), Pfizer
	Pfizer-BioNTech COVID-19 Vaccine (formulated with PBS buffer; available in multiple dose vials with purple caps and labels), Pfizer
	Pfizer-BioNTech COVID-19 Vaccine (formulated with Tris buffer; available in multiple dose vials with gray caps and labels), Pfizer

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