COVID-19 Vaccine, Viral Vector (Janssen)

80:12 • Vaccines (AHFS primary)

Special Alerts:

On April 23, 2021, after a thorough safety review, the FDA and CDC announced that the temporary pause in the use of the Janssen COVID-19 vaccine (also known as the Johnson & Johnson COVID-19 vaccine) in the US was lifted and use of the vaccine should resume. The pause had been initiated on April 13, 2021 out of an abundance of caution to allow time for FDA and CDC to investigate cases of cerebral venous sinus thrombosis (CVST) with thrombocytopenia that had been reported rarely following administration of the vaccine. The pause in use of the vaccine also helped ensure that vaccine recipients and healthcare providers were aware of possible symptoms and that healthcare providers were informed about appropriate management of this extremely rare adverse event. At the time the pause was initiated, more than 6.8 million doses of the Janssen COVID-19 vaccine had been administered in the US and there were 6 cases of CVST reported in vaccine recipients, including one fatality; all 6 cases were reported in females 18–48 years of age and occurred within 6–13 days after vaccination.

FDA and CDC evaluated available data and assessed the risk of thrombosis involving large blood vessels (e.g., the cerebral venous sinuses, portal vein, lower extremity veins, pulmonary artery) occurring with thrombocytopenia (also known as thrombosis with thrombocytopenia syndrome [TTS]) in recipients of the Janssen COVID-19 vaccine. At the time of CDC's safety data analysis (April 21, 2021), a total of 15 cases of TTS had been reported and confirmed, including 3 fatalities. These cases all occurred in females 18–59 years of age (median age 37 years), symptom onset was 6–15 days after vaccination (median 8 days), and the clinical course shared features with autoimmune heparin-induced thrombocytopenia. After extensive evaluation of these TTS cases and analyses of the risks and benefits of vaccination with the Janssen COVID-19 vaccine, FDA and CDC determined that the known and potential benefits of the vaccine outweigh its known and potentials risks in adults 18 years of age or older.

Vaccinees should be instructed to immediately seek medical attention if they develop shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurologic symptoms (including severe or persistent headaches or blurred vision), easy bruising, or a diffuse rash consisting of petechiae (pinpoint-like spots) beyond the vaccination site within 3 weeks after receiving the Janssen COVID-19 vaccine. These symptoms are distinct from the commonly reported adverse effects that may be experienced in the first few days following vaccination (e.g., headache, fatigue, muscle aches, nausea) that usually are mild to moderate in severity and last 1–2 days.

Healthcare providers should maintain a high index of suspicion for signs and symptoms of TTS (e.g., severe headache, backache, new neurologic symptoms, severe abdominal pain, shortness of breath, leg swelling, petechiae, new or easy bruising) occurring approximately 1–2 weeks after vaccination in individuals who have received the Janssen COVID-19 vaccine. Based on data regarding the US patients who developed TTS after receiving the Janssen COVID-19 vaccine and data regarding patients in Europe who developed immune thrombotic thrombocytopenia after receiving a different adenoviral-vectored COVID-19 vaccine not available in the US (i.e., AstraZeneca COVID-19 vaccine), the pathogenesis of such adverse effects after vaccination may be associated with platelet-activating antibodies against platelet factor 4 (PF4). FDA and CDC are alerting clinicians that heparin and its derivatives should be avoided when managing thrombotic events and thrombocytopenia that occur following vaccination with the Janssen COVID-19 vaccine and that other anticoagulants and high-dose immune globulin IV should be considered. Consultation with hematology specialists is strongly recommended. Information for clinicians regarding diagnosis and management of vaccine-induced immune thrombotic thrombocytopenia is available from the American Society of Hematology at https://www.hematology.org/covid- 19/vaccine-induced-immune-thrombotic-thrombocytopenia. Additional background information regarding the cases of TTS reported to date in individuals who received the Janssen COVID-19 vaccine is provided in meeting materials from the April 23, 2021 meeting of CDC's Advisory Committee on Immunization Practices (ACIP) that are available at https://www.cdc.gov/vaccines/acip/meetings/index.html.

Individuals and healthcare providers should report adverse events that occur following vaccination with the Janssen COVID-19 vaccine to the Vaccine Adverse Event Reporting System (VAERS) at https://vaers.hhs.gov/reportevent.html.

■ COVID-19 vaccine (Janssen) is a recombinant, replication-incompetent, viral vector (i.e., adenovirus serotype 26 [Ad26] vector) 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 (Janssen) is an adenovirus-vectored vaccine being investigated and used for the prevention of coronavirus disease 2019† (COVID-19) caused by SARS-CoV-2. The Janssen COVID-19 vaccine is one of various COVID-19 vaccines being evaluated for the prevention of COVID-19.

Although efficacy and safety of COVID-19 vaccine (Janssen) have not been definitely established, the vaccine is available under an FDA emergency use authorization (EUA) for active immunization to prevent COVID-19 in individuals 18 years of age or older.

The US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for use of the Janssen COVID-19 vaccine for prevention of COVID-19 in individuals 18 years of age or older. ACIP also made interim recommendations regarding allocation of supplies of COVID-19 vaccines and interim considerations for phased implementation of COVID-19 vaccination and sub-prioritization among recommended populations in the US (available at the CDC website at https://www.cdc.gov/vaccines/covid-19/phased-implementation.html and https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html).

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

Emergency Use Authorization

On February 27, 2021, FDA issued an EUA that permits use of COVID-19 vaccine (Janssen) to prevent COVID-19 in individuals 18 years of age or older. This EUA requires that the vaccine be administered by vaccination providers using a single-dose regimen as described in the EUA (see Dosage under Dosage and Administration) and that vaccination providers participate and comply with the terms and training required by CDC's COVID-19 vaccination program, including monitoring and complying with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and requirements concerning reporting of vaccine administration data to CDC and state/local jurisdiction's Immunization Information System (IIS) or other designated systems.

FDA issued the EUA for COVID-19 vaccine (Janssen) 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 Janssen COVID-19 vaccine may be effective in preventing COVID-19 and, when used under the conditions described in the authorization, the known and potential benefits outweigh the known and potential risks; and there are no adequate, approved, and available alternatives to the emergency use of the vaccine to prevent COVID-19.

Issuance of the EUA for COVID-19 vaccine (Janssen) was based on FDA review of safety and efficacy data from an ongoing phase 3 clinical trial that enrolled 43,783 adults randomized 1:1 to receive the vaccine or saline control. (See Clinical Experience under Uses.)

The EUA for COVID-19 (Janssen) authorizes that distribution of the vaccine will be controlled by the US government, including CDC and/or other designee, for use

consistent with the terms and conditions of the EUA. (See Restricted Distribution under Preparations.)

To mitigate the risks of this unapproved vaccine, the EUA requires that vaccination providers administering the Janssen COVID-19 vaccine comply with certain mandatory requirements. These requirements include providing the recipient or caregiver with information consistent with the EUA fact sheet for recipients and caregivers and ensuring that all vaccination administration errors and all serious adverse events potentially attributable to the vaccine are reported as specified in the EUA fact sheet for healthcare providers. (See EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting under Cautions.)

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

Clinical Experience

Efficacy, safety, and immunogenicity of a single dose of COVID-19 vaccine (Janssen) for the prevention of COVID-19 are being evaluated in an ongoing multicenter, randomized, double-blind, placebo-controlled, phase 3 clinical trial in adults 18 years of age or older (NCT04505722; ENSEMBLE; study 3001). At the time of FDA's efficacy review of the vaccine for the EUA, the efficacy analysis population had been followed for a median of 8 weeks and data indicated that efficacy of a single dose of the Janssen COVID-19 vaccine in preventing protocol-defined moderate to severe/critical COVID-19 in individuals who were seronegative or had an unknown serostatus at baseline was 66.9% when cases occurring at least 14 days after vaccination were considered and 66.1% when cases occurring at least 28 days after vaccination were considered. Efficacy of a single dose of the vaccine in preventing protocol-defined severe/critical COVID-19 was 76.7 or 85.4% when cases occurring at least 14 or 28 days, respectively, after vaccination were considered.

This phase 3 trial enrolled adults in the US, South Africa, Brazil, Chile, Argentina, Colombia, Peru, and Mexico who were randomized 1:1 to receive a single IM dose of the Janssen COVID-19 vaccine (0.5-mL dose containing 5×10^{10} virus particles of recombinant Ad26) or saline placebo, and randomization was stratified by age (18–59 years of age, 60 years of age or older) and presence or absence of comorbidities associated with an increased risk of progression to severe COVID-19. The study protocol allowed for inclusion of participants with stable preexisting medical conditions, defined as disease not requiring substantial change in therapy during the 3 months prior to enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. The co-primary efficacy end points were first occurrence of moderate to severe/critical COVID-19 with onset of symptoms at least 14 days after vaccination and onset at least 28 days after vaccination. The study protocol defined moderate COVID-19 as laboratory-confirmed SARS-CoV-2 infection and any one of the following new or worsening signs or symptoms: respiratory rate 20 breaths/minute or greater; abnormal oxygen saturation (SpO_2) but still greater than 93% on room air at sea level; clinical or radiologic evidence of pneumonia; radiologic evidence of deep-vein thrombosis; or shortness of breath or difficulty breathing *or* any two of the following new or worsening signs or symptoms: fever (38°C or greater); heart rate 90 beats/minute or greater; shaking chills or rigors; sore throat; cough; malaise; headache; muscle pain (myalgia); GI symptoms; new or changing olfactory or taste disorders; or red or bruised appearing feet or toes. Severe/critical COVID-19 was defined as laboratory-confirmed SARS-CoV-2 infection and any one of the following symptoms at any time during the course of observation: clinical signs at rest indicative of severe systemic illness (respiratory rate 30 breaths/minute or greater, heart rate 125 beats/minute or greater, SpO_2 93% or lower on room air at sea level or partial pressure of oxygen/fraction of inspired oxygen [PaO_2/FiO_2] less than 300 mm Hg; respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]); evidence of shock (defined as systolic blood pressure less than 90 mm Hg, diastolic blood pressure less than 60 mm Hg, or requiring vasopressors); significant acute renal, hepatic, or neurologic dysfunction; admission to an intensive care unit (ICU); or death. SARS-CoV-2 testing was molecularly confirmed by a central laboratory based on a positive SARS-CoV-2 viral RNA result using a polymerase chain reaction (PCR)-based test. Final determinations of severe/critical COVID-19 cases were made by an independent adjudication committee.

The co-primary efficacy analysis population of 39,321 adults (19,630 received the Janssen COVID-19 vaccine and 19,691 received placebo) included 38,059 participants seronegative for SARS-CoV-2 at baseline and 1262 participants with unknown serostatus. Demographic and baseline characteristics were similar among participants who received the Janssen COVID-19 vaccine and those who received placebo.

At the time of FDA's review for the EUA, 116 cases of confirmed moderate to severe/critical COVID-19 had occurred in the vaccine group and 348 cases had occurred in the placebo group at least 14 days after vaccination and 66 and 193 cases had occurred in the vaccine and placebo groups, respectively, at least 28 days after vaccination. This corresponded to 66.9% vaccine efficacy in prevention of moderate to severe/critical COVID-19 when considering cases occurring at least 14 days after vaccination and 66.1% vaccine efficacy when considering cases occurring at least 28 days after vaccination. When central laboratory-confirmed and blind-adjudicated cases of severe/critical COVID-19 were evaluated, 14 and 60 such cases had occurred in the vaccine and placebo groups, respectively, at least 14 days after vaccination and 5 and 34 cases had occurred in the vaccine and placebo groups, respectively, at least 28 days after vaccination. This corresponded to 76.7% vaccine efficacy in prevention of severe/critical COVID-19 when considering cases occurring at least 14 days after vaccination and 85.4% vaccine efficacy when considering cases occurring at least 28 days after vaccination. There were no deaths related to COVID-19 reported in recipients of the Janssen COVID-19 vaccine compared with 5 COVID-19-related deaths in placebo recipients.

Exploratory geographic subgroup analyses of vaccine efficacy against moderate to severe/critical COVID-19 and against severe/critical COVID-19 using data for study participants in the US, Brazil, and South Africa were conducted. (See Table 1.) For these subgroup analyses, all COVID-19 cases accrued up to the primary efficacy analysis data cutoff date, including cases confirmed by the central laboratory and cases with documented positive SARS-CoV-2 PCR from a local laboratory that were still awaiting confirmation by the central laboratory, were analyzed. The concordance rate observed up to the data cut-off date between the PCR results from the local laboratory and the central laboratory was 90.3%.

Table 1. Summary of Efficacy of Janssen COVID-19 Vaccine against Moderate to Severe/Critical and against Severe/Critical COVID-19 (ENSEMBLE; Study 3001)

Country	Efficacy against Moderate to Severe/Critical COVID-19	Efficacy against Severe/Critical COVID-19
US	74.4% at least 14 days after vaccination; 72% at least 28 days after vaccination	78% at least 14 days after vaccination; 85.9% at least 28 days after vaccination
Brazil	66.2% at least 14 days after vaccination; 68.1% at least 28 days after vaccination	81.9% at least 14 days after vaccination; 87.6% at least 28 days after vaccination
South America	52% at least 14 days after vaccination; 64% at least 28 days after vaccination	73.1% at least 14 days after vaccination; 81.7% at least 28 days after vaccination

Strain sequencing was conducted on samples obtained from study 3001 participants who had centrally confirmed COVID-19 if viral load was sufficient (one sequence per case). As of February 12, 2021, 71.7% of samples from central laboratory-confirmed primary analysis cases had been sequenced. Results indicated that 96.4% of strains tested from US participants were identified as the Wuhan-H1 variant D614G; 94.5% of strains tested from participants in South Africa were identified as the 20H/501Y.V2 variant (B.1.351 lineage); and 69.4% of strains tested from participants in Brazil were identified as a variant of the P.2 lineage and 30.6% were identified as the Wuhan-H1 variant D614G. As of February 12, 2021, SARS-CoV-2 variants from the B1.1.7 or P.1 lineages were not found in any of the sequenced samples from study participants.

Dosage and Administration

■ General

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

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

All individuals who receive a COVID-19 vaccine should be monitored for immediate adverse reactions according to CDC (ACIP) guidelines. When individuals with no contraindications to vaccination with the Janssen COVID-19 vaccine receive the vaccine, ACIP states that those with a history of an immediate allergic reaction of any severity to any other vaccine or injectable therapy and those with a history of anaphylaxis due to any cause not considered a contraindication should be observed for 30 minutes after receiving the vaccine, and that all other individuals should be observed for 15 minutes. A longer period of observation may be indicated for some individuals based on clinical concern (e.g., vaccinee develops pruritus and swelling confined to the injection site during their observation period). Vaccine recipients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site. (See Hypersensitivity Reactions under Cautions.)

Syncope (vasovagal or vasodepressor reaction; fainting) may occur following administration of parenteral vaccines; such reactions usually occur within 15 minutes

following vaccine administration and are reported most frequently in adolescents and young adults. Appropriate measures should be taken to decrease the risk of injury if a patient becomes weak or dizzy or loses consciousness (e.g., vaccinees should sit or lie down during and for 15 minutes after vaccination). If syncope occurs, the patient should be observed until symptoms resolve.

At the time that the Janssen COVID-19 vaccine is administered, vaccine recipients or their caregivers should be given a vaccination record card that provides the name of the vaccine (Janssen COVID-19 vaccine) and the date the vaccine was administered.

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

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

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

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

■ Administration

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

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

IM Injection

COVID-19 vaccine (Janssen) is supplied as a suspension in multiple-dose vials.

Although the Janssen COVID-19 vaccine is *initially* stored frozen by the manufacturer, the vaccine is shipped and stored refrigerated at a temperature of 2–8°C. (See Stability.)

The Janssen COVID-19 vaccine should not be diluted.

After removal from refrigeration, unused vials (i.e., unpunctured) may be stored for up to 12 hours at room temperature (9–25°C). After the first dose of Janssen COVID-19 vaccine is withdrawn from the multiple-dose vial, the vial should be held in a refrigerator (2–8°C) for up to 6 hours or at room temperature (up to 25°C) for up to 2 hours and *must* be discarded if not used within these time frames after first vial entry. The date and time of first use should be recorded on the vial label.

Before withdrawing each dose, the vaccine vial should be gently swirled in an upright position for 10 seconds and should *not* be shaken.

The Janssen COVID-19 vaccine should appear as a colorless to slightly yellow, clear to very opalescent suspension and should *not* be used if it is discolored or contains particulates.

To administer a dose of the Janssen COVID-19 vaccine, 0.5 mL of the vaccine should be withdrawn from the vial using aseptic technique and an appropriate syringe and needle and administered immediately.

Each multiple-dose vial of Janssen COVID-19 vaccine provides five 0.5-mL doses. Because the vaccine does not contain preservatives, it is critical that any vaccine remaining in the vial that does not constitute a full 0.5-mL dose should be discarded and should *not* be pooled with vaccine from other vials to create a dose.

■ Dosage

COVID-19 vaccine (Janssen) is administered as a single 0.5-mL dose. The 0.5-mL dose contains 5×10^{10} virus particles of recombinant, replication-incompetent Ad26 (see Description).

Janssen COVID-19 vaccine is *not* interchangeable with any other COVID-19 vaccine.

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

Safety and efficacy regarding use of the Janssen COVID-19 vaccine after a dose of an mRNA COVID-19 vaccine have *not* been established. However, ACIP states that, in limited, *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the vaccination series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), a single dose of Janssen COVID-19 vaccine administered at least 28 days after the first dose of mRNA COVID-19 vaccine may be considered. (See Hypersensitivity Reactions under Cautions.) An individual who receives a single dose of Janssen COVID-19 vaccine after a dose of an mRNA COVID-19 vaccine under such exceptional circumstances should be considered to have received valid, single-dose vaccination with Janssen COVID-19 vaccine, not a mixed vaccination series.

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

Adult Dosage

The FDA EUA that permits use of COVID-19 vaccine (Janssen) for the prevention of COVID-19† (see Emergency Use Authorization under Uses) states that adults 18 years of age or older should receive a single 0.5-mL dose of the vaccine.

Cautions

■ Contraindications

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

■ Warnings/Precautions

Sensitivity Reactions

Hypersensitivity Reactions.

At the time that FDA's safety analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating COVID-19 vaccine (Janssen) was performed for the EUA, urticaria (nonserious) occurring within 7 days following vaccination had been reported in 5 individuals who received the vaccine and 1 individual who received placebo.

A serious adverse hypersensitivity event (not classified as anaphylaxis) was reported in one vaccinated individual; the reaction consisted of urticaria beginning 2 days following vaccination and angioedema of the lips beginning 4 days following vaccination without respiratory distress. This event was considered likely related to the vaccine.

Severe allergic reactions, including one case of anaphylaxis, have been reported in an ongoing open-label study in South Africa.

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 COVID-19 vaccination are consistent with immediate allergic reactions or are reactions commonly observed following vaccination, such as vasovagal reactions or postvaccination adverse effects.

History of polysorbate allergy: This a **contraindication** to vaccination with COVID-19 vaccine (Janssen). ACIP states that use of an mRNA COVID-19 vaccine (Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine) can be considered in such individuals. However, polysorbates are structurally related to polyethylene glycol (PEG), an ingredient in mRNA COVID-19 vaccines, and there is potential for cross-reactive hypersensitivity with PEG. Consultation with an allergist-immunologist should be considered to help determine if the individual with polysorbate allergy can safely receive an mRNA COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html) when making such decisions.

Known contraindication to vaccination with mRNA COVID-19 vaccines (including known PEG allergy): ACIP considers this a **precaution** to vaccination

with COVID-19 vaccine (Janssen) and states that consideration can be given to using the Janssen COVID-19 vaccine in such individuals. However, because of potential cross-reactive hypersensitivity between ingredients in mRNA COVID-19 vaccines and the Janssen COVID-19 vaccine (including PEG and polysorbate 80, respectively), consultation with an allergist-immunologist should be considered to help determine if the individual can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments can also request a clinical consultation from the Clinical Immunization Safety Assessment COVIDvax project (https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html) when making such decisions. If a decision is made to administer the Janssen COVID-19 vaccine to individuals with a contraindication to mRNA COVID-19 vaccines, the vaccine should be administered *only* in an appropriate setting under the supervision of a healthcare provider experienced in the management of severe allergic reactions. Although safety and efficacy of administering COVID-19 vaccine (Janssen) after an mRNA COVID-19 vaccine has not been established, ACIP states that in those *exceptional* situations when an individual received the first dose of an mRNA COVID-19 vaccine but is unable to complete the series with either the same or different mRNA COVID-19 vaccine (e.g., due to a contraindication), a single dose of the Janssen COVID-19 vaccine may be considered at a minimum interval of 28 days after the mRNA COVID-19 vaccine dose. (See Dosage under Dosage and Administration.)

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

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

History of allergic reactions (including severe allergic reactions) not related to COVID-19 vaccines or 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. In addition, allergies to eggs or gelatin are **not** a contraindication or precaution since COVID-19 vaccines do not contain eggs or gelatin.

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

When a COVID-19 vaccine, including the Janssen COVID-19 vaccine, is administered to individuals without a contraindication to such vaccines, ACIP states that those with a history of an immediate allergic reaction of any severity to any other vaccine or injectable therapy and those with a history of anaphylaxis due to any cause not considered a contraindication should be observed for 30 minutes after the vaccine dose, and that all other individuals should be observed for 15 minutes. Vaccine recipients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination site.

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

ACIP interim guidance regarding early recognition of clinical signs and symptoms of anaphylaxis and guidance regarding preparation for and management of anaphylaxis at COVID-19 vaccination sites, including recommendations for medications and supplies to have immediately available and specific recommendations regarding therapeutic management of anaphylaxis, are available at the CDC website at https://www.cdc.gov/vaccines/covid-19/clinicalconsiderations/managing-anaphylaxis.html and https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html.

When confronted with a complex COVID-19 vaccine safety question concerning an individual patient that is not readily addressed by ACIP guidance, US healthcare personnel 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).

Concomitant Illness

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

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

Individuals with Prior SARS-CoV-2 Infection.

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

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

Individuals with Current SARS-CoV-2 Infection.

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

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

Individuals with Recent Exposure to SARS-CoV-2 Infection.

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

Individuals in the community or outpatient setting with a known COVID-19 exposure: ACIP states that such individuals should not seek COVID-19 vaccination until their quarantine period has ended to avoid potentially exposing healthcare personnel and other individuals to SARS-CoV-2 during the vaccination visit.

Individuals residing in congregate healthcare settings (e.g., long-term care facilities) or congregate non-healthcare settings (e.g., correctional and detention facilities, homeless shelters) with a known COVID-19 exposure: ACIP states that such individuals may receive COVID-19 vaccination since exposure to and transmission of SARS-CoV-2 can occur repeatedly for long periods of time in these settings and healthcare personnel and other staff are already in close contact with residents in these settings. Individuals providing vaccination services should employ appropriate infection prevention and control procedures.

Residents in congregate settings (healthcare and non-healthcare) with a known COVID-19 exposure waiting for results of SARS-CoV-2 testing: ACIP states that such individuals may receive COVID-19 vaccination if they do not have symptoms consistent with COVID-19. Individuals providing vaccination services should employ appropriate infection prevention and control procedures. Viral testing to assess for acute SARS-CoV-2 infection solely for the purpose of COVID-19 vaccination decision-making is *not* recommended. (See Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals under Cautions.)

Individuals with Underlying Medical Conditions

ACIP states that individuals with altered immunocompetence or certain underlying medical conditions may receive COVID-19 vaccination if they have no contraindications to the vaccine. ACIP does not state a preference for any specific COVID-19 vaccine in such individuals. Clinical trials of COVID-19 vaccines have demonstrated that safety and efficacy profiles in individuals with some underlying medical conditions, including those that place them at increased risk for severe COVID-19, are similar to safety and efficacy profiles in individuals without comorbidities.

Individuals with Altered Immunocompetence.

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

Although some individuals with altered immunocompetence (e.g., HIV infection) have been included in the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the Janssen COVID-19 vaccine, the number of such individuals has been insufficient to evaluate safety of the vaccine in such populations.

ACIP states that individuals with HIV infection or other immunocompromising conditions and individuals receiving immunosuppressive therapies may be at increased risk for severe COVID-19 and, although data are not currently available to establish safety and efficacy in such individuals, they may receive any authorized COVID-19 vaccine if they have no contraindications to the vaccine. However, such individuals 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 guidelines to protect themselves from COVID-19.

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

Individuals with Autoimmune Conditions.

ACIP states that individuals with autoimmune conditions may receive any authorized COVID-19 vaccine, unless they have a contraindication to the vaccine. Although data are not currently available regarding the safety and efficacy of COVID-19 vaccines in individuals with autoimmune conditions, such individuals were not excluded from clinical trials evaluating the mRNA COVID-19 vaccines and these trials showed no imbalances in the occurrence of symptoms consistent with autoimmune conditions or inflammatory disorders in trial participants who received COVID-19 vaccine compared with those who received placebo.

Individuals with Liver Disease.

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

Although safety and efficacy data regarding use of COVID-19 vaccines in individuals with chronic liver disease are limited and additional studies are needed, safety and efficacy of the vaccines in such individuals are expected to be similar to the general population. AASLD states that individuals with chronic liver disease who are receiving antiviral treatment for hepatitis B virus (HBV) or hepatitis C virus (HCV) infection and those receiving medical therapy for primary biliary cholangitis or autoimmune hepatitis should not discontinue such therapy when receiving COVID-19 vaccination. In addition, patients with hepatocellular carcinoma undergoing locoregional or systemic therapy should be considered for COVID-19 vaccination without interruption of treatment.

AASLD states that liver transplant candidates should receive COVID-19 vaccination prior to transplantation, whenever possible, to help ensure an adequate immune response. The best time for COVID-19 vaccination in previously unvaccinated liver transplant recipients is likely to be at least 3 months after transplant; however, vaccination may be given as early as 6 weeks after transplant if indicated based on ongoing community spread of SARS-CoV-2, especially in those at highest risk with other comorbid factors associated with severe COVID-19.

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

Individuals with a History of Guillain-Barré Syndrome.

Data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the Janssen COVID-19 vaccine identified a single case of Guillain-Barré syndrome (GBS) that occurred in a vaccine recipient 16 days after the vaccine dose and a single case in a placebo recipient that occurred 10 days after the dose. FDA stated that, although the case of GBS was unlikely to be related to the vaccine, a causal relationship cannot be definitively excluded.

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

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

Individuals with a History of Bell's Palsy.

Data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial evaluating the Janssen COVID-19 vaccine identified 2 cases of Bell's palsy (facial paralysis) in the vaccine group and 2 cases in the placebo group. FDA stated that, although the cases of Bell's palsy were unlikely to be related to the vaccine, a causal relationship cannot be definitively excluded.

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

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

Individuals with Increased Bleeding Risk.

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

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

Individuals receiving anticoagulation therapy presumably have the same bleeding risk as patients with clotting factor disorders and should follow the same guidelines for IM administration. If possible, IM vaccines could be scheduled prior to use of an anticoagulant so that the patient's risk of bleeding is not increased by the drug's therapeutic action.

Thromboembolic Events and Other Adverse Events

At the time that FDA's safety analysis of the phase 3 trial of the Janssen COVID-19 vaccine was performed for the EUA, there had been 6 reports of deep-vein thrombosis in individuals who received the vaccine (2 serious events; 5 events within 28 days of vaccination) and 2 such events in placebo recipients (1 serious; 2 within 28 days of vaccination). In addition, there were 4 reports of pulmonary embolism (3 serious; 2 within 28 days of vaccination) in vaccine recipients versus 1 report in placebo recipients (serious; within 28 days of vaccination) and 1 report of transverse sinus thrombosis (serious; within 28 days of vaccination) in vaccine recipients versus none in placebo recipients. A causal relationship between these thromboembolic events and the vaccine could not be established based on the phase 3 trial data. However, thrombosis involving large blood vessels (e.g., the cerebral venous sinuses, portal vein, lower extremity veins, pulmonary artery) occurring with thrombocytopenia have been reported rarely during post-authorization surveillance (see Special Alert at the beginning of the monograph) and evaluation of these cases suggest that a causal relationship between the Janssen COVID-19 vaccine and thrombosis with thrombocytopenia is plausible.

Other adverse effects with a numerical imbalance between vaccine recipients and placebo recipients included 4 reports of seizures in vaccine recipients (1 serious; 4 within 28 days of vaccination) versus 1 seizure event in placebo recipients and 6 reports of tinnitus in vaccine recipients (not serious; all 6 within 28 days of vaccination, including 3 within 2 days of vaccination) versus none in placebo recipients. A causal relationship between these events and the vaccine could not be established.

Limitations of Vaccine Effectiveness

COVID-19 vaccine (Janssen) may not protect all vaccine recipients 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 a COVID-19 vaccine would provide an adequate immune response within the incubation period for effective postexposure prophylaxis.

FDA states that data are too limited to date to assess the effect of the Janssen COVID-19 vaccine for prevention of asymptomatic SARS-CoV-2 infection; additional evaluations are needed, including data from clinical trials and from use of the vaccine after issuance of the EUA.

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

Based on the currently limited information on the extent to which vaccination may reduce viral transmission in the general population and the unknown duration of vaccine-induced protection, individuals who receive COVID-19 vaccination should be counseled to follow current guidance to protect themselves and others. This includes wearing a mask, staying at least 6 feet away from others, avoiding crowds, avoiding poorly ventilated spaces, covering coughs and sneezes, washing hands frequently, following CDC travel guidance, and following any applicable workplace or school guidance. CDC has issued interim public health recommendations for individuals who are fully vaccinated against COVID-19 (defined as at least 2 weeks after a single dose of the Janssen COVID-19 vaccine or at least 2 weeks after completion of a 2-dose vaccination series of the Moderna COVID-19 vaccine or Pfizer-BioNTech COVID-19 vaccine); these recommendations (available at the CDC website at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html) should be consulted for information on precautionary measures that fully vaccinated individuals should take in various social situations and/or following exposure to someone with suspected or confirmed COVID-19.

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

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

Duration of Immunity

The duration of protection against SARS-CoV-2 infection following vaccination with a single dose of COVID-19 vaccine (Janssen) has not been fully evaluated.

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

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

Improper Storage and Handling

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

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

If there are concerns about mishandling or defective or damaged vaccine, the manufacturer should be contacted at 800-565-4008 for guidance.

EUA Requirements for Postvaccination Monitoring and Mandatory Vaccine Adverse Event Reporting

Safety and efficacy of COVID-19 vaccine (Janssen) have not been established. The FDA issued an EUA that permits use of the vaccine for the prevention of COVID-19† in individuals 18 years of age or older when administered according to the single-dose regimen specified in the EUA. (See Emergency Use Authorization under Uses.)

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

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

Vaccine recipients or their caregivers should be provided with information on, and encouraged to participate in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received a COVID-19 vaccine to identify potential adverse effects. Reports to v-safe that indicate a medically important health impact are followed up by the CDC v-safe call center to collect additional information to complete a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

It is mandatory that vaccination providers administering COVID-19 vaccine (Janssen) report all vaccine administration errors (even if not associated with an adverse event) and serious adverse events (irrespective of attribution to vaccination) that occur following vaccination and also report all cases of multisystem inflammatory syndrome (MIS) and COVID-19 that result in hospitalization or death in vaccine recipients to VAERS. VAERS reports can be completed and submitted online at https://vaers.hhs.gov/reportevent.html or faxed to 877-721-0366; the words "Janssen 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 (Janssen) at JNJvaccineAE@its.jnj.com (email), 215-293-9955 (fax), or 800-565-4008 (phone).

The FDA fact sheet for healthcare providers for the Janssen COVID-19 vaccine available at the FDA website and at http://www.janssencovid19vaccine.com should be consulted for requirements and instructions regarding reporting of adverse reactions and vaccination errors.

Interpretation of SARS-CoV-2 Testing in Vaccinated Individuals

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

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

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

Interpretation of Tuberculosis Tests in Vaccinated Individuals

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

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

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

Specific Populations

Pregnancy.

Data are insufficient to date regarding use of COVID-19 vaccine (Janssen) in pregnant women to inform vaccine-associated risks during pregnancy. In a reproductive developmental toxicity study in female rabbits, there was no evidence of vaccine-related adverse effects on female fertility, embryofetal development, or postnatal development up to postnatal day 28 when 1 mL of the Janssen COVID-19 vaccine was given by IM injection 7 days prior to mating and on gestation days 6 and 20 (i.e., during early and late gestation, respectively).

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

Although data are limited regarding the safety of the Janssen COVID-19 vaccine during pregnancy, a different adenovirus-vectored vaccine (i.e., Ebola virus vaccine not available in the US) has been used in a large-scale vaccination trial that included pregnant women who were vaccinated during any trimester and no adverse pregnancy-related outcomes, including infant outcomes, were identified that were determined to be related to the vaccine.

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

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

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

ACIP and ACOG state that a conversation between the pregnant woman and her clinical team may assist with decisions regarding use of COVID-19 vaccines available under an EUA; however, such a conversation is not required prior to vaccination. When making a decision, these experts recommend that the pregnant woman and her

healthcare provider consider the level of COVID-19 transmission in the community, the individual's personal risk of contracting COVID-19, risks of COVID-19 to the individual and potential risks to the fetus, efficacy of the vaccine, adverse effects of the vaccine, and limited data about use of the vaccine during pregnancy.

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

Administration of other vaccines (e.g., diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed [DTaP], influenza vaccine) in pregnant women should be deferred for 14 days after COVID-19 vaccination. (See Vaccines under Drug Interactions.) ACOG states that 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.)

A pregnancy exposure registry to monitor pregnancy outcomes in women exposed to the Janssen COVID-19 vaccine during pregnancy has been established. Women who are vaccinated with the Janssen COVID-19 vaccine during pregnancy are encouraged to enroll in the registry at https://c-viper.pregistry.com.

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

Females and Males of Reproductive Capacity.

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

ACIP states that women trying to become pregnant do not need to avoid pregnancy after COVID-19 vaccination.

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

There is no evidence that any of the authorized COVID-19 vaccines affect future fertility.

Lactation.

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

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

ACIP states that COVID-19 vaccines are not thought to be a risk for breast-feeding women or their infants and any of the currently authorized COVID-19 vaccines can be administered to breast-feeding women. ACIP does not state a preference for any specific COVID-19 vaccine in such women.

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

Pediatric Use.

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

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

Geriatric Use.

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

At the time that FDA's safety analysis of data from the ongoing randomized, double-blind, placebo-controlled, phase 3 trial was performed for the EUA, 19.5% of participants were 65 years of age and older and 3.7% were 75 years of age and older. No overall differences in safety or efficacy were observed between adults 65 years of age and older and younger individuals.

■ Common Adverse Effects

Data regarding the safety of COVID-19 vaccine (Janssen) are available from several clinical trials, including the ongoing randomized, double-blind, placebo-controlled, phase 3 trial (NCT04505722; ENSEMBLE; study 3001) evaluating a single dose of the vaccine. At the time that FDA's safety analysis of the phase 3 trial was performed for the EUA, a total of 43,783 study participants 18 years of age or older had been followed for 2 months (21,895 in the vaccine group). A subset of 6736 participants (3356 in the vaccine group and 3380 in the placebo group) were followed for solicited local and systemic adverse effects within 7 days following vaccination and unsolicited adverse effects within 28 days following vaccination.

Solicited local adverse effects reported in vaccine recipients included injection site pain (48.6%), erythema (7.3%), and swelling (5.3%). Onset of local adverse effects generally occurred within the first 1–2 days after vaccination, and the median duration of symptoms was 2 days. However, pain was reported to last longer than 7 days in 2.3% of vaccine recipients and erythema and swelling lasted longer than 7 days in 0.5–0.8% of vaccinees.

Solicited systemic adverse effects reported in vaccine recipients included headache (38.9%), fatigue (38.2%), myalgia (33.2%), nausea (14.2%), and fever (9%). Onset of systemic adverse effects generally occurred within the first 1–2 days after vaccination, and the median duration of symptoms was 1–2 days.

Use of antipyretics/analgesics within 7 days following vaccination was reported in 19.9% of vaccine recipients versus 5.7% of placebo recipients.

Solicited adverse local and systemic reactions generally were reported more frequently in vaccinees 18–59 years of age than in vaccinees 60 years of age or older.

At the time that FDA's safety analysis of the ongoing phase 3 trial was performed for the EUA, serious adverse events (excluding those related to confirmed COVID-19) had been reported in 0.4% of vaccine recipients and 0.4% of placebo recipients. Severe allergic reactions, including anaphylaxis, have been reported rarely. (See Hypersensitivity Reactions under Cautions.)

Drug Interactions

■ 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 a COVID-19 vaccine, either concurrently with or at any interval before or after the immune globulin or antibody therapy since such products are unlikely to substantially impair immune responses to the COVID-19 vaccine. ACIP states that there is no recommended minimum interval between receipt of antibody therapies not specific for SARS-CoV-2 and COVID-19 vaccination.

SARS-CoV-2 Antibody Therapies

Data are not available regarding the safety and efficacy of administering COVID-19 vaccines to individuals who have received passive antibody therapy with investigational SARS-CoV-2-specific monoclonal antibodies (e.g., bamlanivimab, bamlanivimab and etesevimab, casirivimab and imdevimab) or investigational COVID-19 convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of SARS-CoV-2 antibody therapies as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, ACIP recommends that COVID-19 vaccination should be deferred for at least 90 days after such therapies as a precautionary measure until additional information becomes available since this avoids potential interference of the antibody therapy with immune responses to the COVID-19 vaccine. 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 has been vaccinated with a COVID-19 vaccine subsequently develops COVID-19, ACIP states that prior receipt of a 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 Janssen 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 a COVID-19 vaccine if they have no contraindications to vaccination. (See Individuals with Altered Immunocompetence under Cautions.)

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

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

■ Vaccines

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

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

Description

COVID-19 vaccine (Janssen) is a viral vector vaccine composed of a recombinant, replication-incompetent, human adenovirus type 26 (Ad26) vector encoding the SARS-CoV-2 spike (S) protein in a stabilized conformation. The Ad26 vector expressing the SARS-CoV-2 S protein is grown in PER.C6 TetR cells, in media containing amino acids and no animal-derived proteins.

Following IM injection of the Janssen COVID-19 vaccine, the Ad26 vector enters human cells and expresses the S antigen of SARS-CoV-2 (without virus propagation). An immune response to the S antigen is then elicited to protect against SARS-CoV-2 infection.

Data from an ongoing phase 1/phase 2 clinical trial in healthy adults 18 years of age or older indicate that a single dose of Janssen COVID-19 vaccine containing 5×10^{10} virus particles (i.e., recombinant Ad26) elicited SARS-CoV-2 neutralizing antibody when tested against wild-type virus and a SARS-CoV-2 S-binding antibody response that was detected by day 15 after the dose and was increased when evaluated at day 57. The vaccine dose elicited cellular responses in study participants that were consistent with a Th-1 phenotype. A second dose of the vaccine given 56 days after the first dose resulted in increased naturalizing antibody titers.

COVID-19 vaccine (Janssen) available for use under the FDA EUA is provided as a suspension in multiple-dose vials. Each 0.5-mL dose of COVID-19 vaccine (Janssen) contains 5×10^{10} virus particles (i.e., recombinant Ad26). Each dose of the vaccine also contains citric acid monohydrate, trisodium citrate dihydrate, ethanol, 2-hydroxypropyl-β-cyclodextrin (HBCD), polysorbate 80, and sodium chloride. Each dose may also contain residual amounts of host cell proteins and/or host cell DNA.

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

Advice to Patients

Prior to administration of COVID-19 vaccine (Janssen), the vaccine recipient or their caregiver must be provided with information consistent with the Fact Sheet for Recipients and Caregivers: Emergency Use Authorization (EUA) of the Janssen COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 18 Years of Age or Older and given a copy of the fact sheet or directed to the manufacturer's website at http://www.janssencovid19vaccine.com to obtain the fact sheet.

Give the vaccine recipient or their caregiver a vaccination card that provides the name of the vaccine (Janssen COVID-19 vaccine) and the date the vaccine was administered.

Provide the vaccine recipient or their caregiver with information on, and encourage participation in, CDC's voluntary smartphone-based tool (v-safe) that uses text messaging and web surveys to check in with individuals who have received a COVID-19 vaccine to identify potential adverse effects; live telephone follow-up is provided if a medically important health impact is reported. Information on v-safe is available at https://www.cdc.gov/vsafe.

Inform vaccine recipients or their caregivers that FDA authorized the emergency use of the Janssen COVID-19 vaccine, which is an investigational vaccine that has not received FDA approval, for use in individuals 18 years of age or older. Advise them that an ongoing clinical trial has shown that a single dose of the vaccine can prevent COVID-19; however, the duration of protection following vaccination is unknown and the vaccine may not protect everyone who receives it.

Inform vaccine recipients or their caregivers that they have the option to accept or refuse the vaccine.

Provide vaccine recipients or their caregivers with information on available alternative vaccines and the risks and benefits of those alternatives.

Inform vaccine recipients or their caregivers about the significant known and potential risks and benefits of the Janssen COVID-19 vaccine, and the extent to which such risks and benefits are unknown. Inform them that local adverse effects (injection site pain, swelling, redness) and systemic adverse effects (headache, fatigue, muscle aches, nausea, fever) have been reported in recipients of the Janssen COVID-19 vaccine.

Importance of vaccine recipient informing the vaccination provider of any allergies or fever. Advise vaccine recipients or their caregivers that there is a remote chance that the vaccine could cause a severe allergic reaction and such reactions would usually occur within a few minutes to 1 hour after receiving the vaccine 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 previously received any other COVID-19 vaccine, have any medical conditions (e.g., bleeding disorders, immunocompromising diseases), or are receiving anticoagulants or immunosuppressive therapy.

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

Overview® (see Users Guide). It is *essential* that the Emergency Use Authorization (EUA) prescribing information contained in the Fact Sheet for Healthcare Providers that is available at the FDA website and at http://www.janssencovid19vaccine.com be consulted for more detailed information on dosage and administration, cautions, precautions, and contraindications, and for complete information on the conditions for use of the vaccine for the prevention of coronavirus disease 2019 (COVID-19) under the EUA, including mandated record keeping and reporting requirements.

Preparations

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

COVID-19 vaccine (Janssen) is not commercially available. FDA issued an emergency use authorization (EUA) for the Janssen COVID-19 vaccine that permits use of the vaccine for the prevention of COVID-19† in individuals 18 years of age or older. Allocation of the vaccine for use under the EUA is being directed by the US government. The vaccine will be supplied directly from the manufacturer or authorized US distributor(s) and distributed to emergency response stakeholders as directed by the US government, including the CDC and/or other designee.

COVID-19 Vaccine, Viral Vector (Janssen)

Parenteral

Suspension, for IM use

5×10^{10} virus particles (recombinant Adenovirus type 26) per 0.5-mL dose

Janssen COVID-19 Vaccine, Janssen

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