



December 14, 2020

****Emergency Use Authorization****

Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)

Vaccine Platform & Mechanism of Action¹: Messenger RNA (mRNA)-based vaccine; mRNA vaccines introduce mRNA that encodes a disease-specific antigen, in this case the SARS-CoV-2 spike protein (which helps the virus attach to and invade cells), and leverage the host cells' protein synthesis machinery to produce antigens that elicit the immune response. The production of these foreign antigens prepares the immune system to recognize this viral antigen so it is ready to combat future infections caused by virus with the same antigen.

Current Status²: On December 11, 2020, the U.S Food and Drug Administration issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 Vaccine for prevention for COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. It is not currently FDA-approved for any indication.

Availability³: The U.S. government pre-purchased 100 million doses from the manufacturer in July 2020; distribution of vaccine supply is underway, following the EUA.

Recommended Administration & Storage⁴: The vaccine (30 micrograms) is administered intramuscularly (IM) as a series of two 30 microgram doses of the diluted vaccine solution (0.3 mL each) according to the following schedule: a single dose (DAY 1) followed by a second dose 21 days later (DAY 21).

Ultralow temperature containers are used to ship the vaccine and should be replenished within 24 hours of initial receipt with dry ice. Once replenished, the shipping container can be used as temporary storage as long as dry ice is replenished every 5 days (120 hours) thereafter. The vaccine is supplied as a multiple-dose (5-dose) vial containing a frozen (between -80°C to -60°C) suspension that is preservative-free. The vaccine must be thawed and diluted in its original vial with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to administration – DO NOT SHAKE. After dilution, the vial contains 5 doses of 0.3 mL per dose. Following dilution, the multiple-dose vials must be stored between 2°C to 25°C and must be used within 6 hours from the time of dilution. More information and resources are available in the [CDC Vaccine Storage & Handling Toolkit](#).

Efficacy⁵: Study C4591001 is an ongoing, randomized and placebo-controlled Phase 1/2/3 study. It began as a Phase 1/2 study in the US, then expanded to a global Phase 2/3 study enrolling nearly 44,000 participants. The Phase 3 clinical trial began on July 27 with approximately 42% of global study participants (30% of US participants) of racially and ethnically diverse backgrounds. American Indians or Alaskan Natives represented <1% of all study participants.

Final analysis of the primary efficacy outcome (43,252 participants) yielded 170 confirmed cases of COVID-19 occurring at least 7 days after Dose 2, with 162 cases in the placebo group vs. 8 cases in the vaccine group, providing a statistically significant 95% vaccine efficacy rate compared to placebo ($p < 0.0001$). The 95% credible interval for vaccine efficacy (VE) was 90.3% to 97.6%, indicating that the true VE is at least 90.3%, with a 97.5% probability. Researchers reported 10 severe cases of COVID-19 in the trial, 9 of which occurred in the placebo group. Also, early onset of protection against COVID-19 occurrence appears at approximately Day 14 after the first dose. Lastly, VE remained high (>94%) in participants with or without known prior SARS-CoV-2 infection.

The study was ethnically diverse, and results were consistent across gender and age groups, with a 94% efficacy reported among participants older than 65. Observed VE was >93% for the first primary efficacy endpoint across subgroups of age, sex, race/ethnicity, and country, with the exception of "all others" race group (89.3% VE) and Brazil (87.7% VE).

Reactogenicity & Adverse Events (AEs)^{6,7}: According to decades of FDA vaccine experience, more than 90% of side effects appear within 40 days of administration. Data from ~38,000 participants with a median follow-up of 2 months after Dose 2 show that the Pfizer-BioNTech COVID-19 Vaccine was safe and well-tolerated in participants ≥16 years of age. Reactogenicity and AEs were generally milder and less frequent in participants in the older group (≥56 years of age) compared with younger patients (≤55 years of age). Reactogenicity was mostly mild to moderate and short-lived after dosing. It is important to note that individuals with medical conditions considered to confound evaluation of vaccine safety or immunogenicity were excluded from the study (i.e., patients with a history of significant allergic reactions). Data reported however show small numbers of allergic reactions overall in both the vaccine and placebo trial groups (0.63% and 0.51%) comparatively.

In the all enrolled participant population (N= 43,252), incidences of serious AEs and deaths were low and comparable between the vaccine and placebo groups, and incidence of discontinuations due to AEs was also low and similar between groups (0.2% vs 0.1%). The most frequently reported AEs in the vaccine group were injection site pain, pyrexia, chills, fatigue, headache, and myalgia. Additionally, systemic events (i.e., fever, chills, fatigue, headache) were increased in frequency and severity in the vaccine younger group compared with the older group, with frequencies and severity increasing with number of doses (dose 1 vs dose 2).

CDC Advisory Committee on Immunization Practices (ACIP)^{8,9}: On December 12, 2020, the ACIP voted unanimously to recommend use of the Pfizer-BioNTech mRNA vaccine in individuals 16 years or older in the United States, stating it was safe and effective. The review included important clinical considerations. The panel also voted unanimously to include the vaccine in 2021 immunization schedules.

COVID-19 Vaccination Resource Compendium:

- Healthcare Professionals: [Preparing for COVID-19 Vaccination](#), including:
 - [Vaccine Storage & Handling Toolkit](#)
 - [Training Module for HealthCare Professionals](#)
 - [Training Programs and Reference Materials for Healthcare Professionals](#)
- Adverse Vaccine Event Reporting: [Vaccine Adverse Event Reporting System \(VAERS\)](#)
- General Vaccination Information & Training:
 - [Vaccine Storage and Handling](#) – resources, toolkit, videos
 - [Vaccine Administration](#) –training materials, vaccine documentation, videos, VAERS
 - [Resource Library](#) – e-learning, videos, job aids, references
 - [Planning Mass Vaccination Clinics](#) – For off-site, satellite or temporary locations

Patient Education¹⁰:

*****Key Points and Materials to Share with Patients*****

1. Various patient education documents are available from the CDC including:
 - [COVID-19 Vaccination Communication Toolkit](#) (for Medical Centers, Clinics, and Clinicians)
 - [Talking to Patients about COVID-19 Vaccines](#)
 - [Understanding mRNA COVID-19 Vaccines](#)
 - [Making a Strong Recommendation for COVID-19 Vaccination](#)
2. In addition to the CDC patient education hyperlinks above, key messages to share with patients include:
 - *Like all vaccines, COVID-19 mRNA vaccines have been rigorously tested for safety before being authorized for use in the United States.*
 - *mRNA technology is new, but not unknown. They have been studied for more than a decade.*
 - *mRNA vaccines don't contain a live virus and don't carry a risk of causing disease in a vaccinated person.*
 - *Vaccine mRNA never enters the nucleus of the cell and does not affect or interact with a person's DNA.*
3. Discuss and provide the enrollment process for the [CDC "v-safe" vaccine monitoring smartphone tool](#)

References:

1. Li, Yingzhu. American Chemical Society blog. [Meet the mRNA vaccine rookies aiming to take down COVID-19](#). Accessed 11-30-20.
2. FDA NEWS RELEASE. [FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine](#)
3. Department of Health & Human Services. Operation Warp Speed. [Fact Sheet: Explaining Operation Warp Speed](#). Assessed Dec 11, 2020.
4. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. [Emergency Use Authorization of Pfizer-BioNTech Vaccine](#).
5. Polack FP, et al. [Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine](#). NEJM. 2020; DOI: 10.1056/NEJMoa2034577
6. PFIZER-BIONTECH COVID-19 VACCINE (BNT162, PF-07302048) VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE [BRIEFING DOCUMENT](#).
7. Medscape Medical News. [COVID-19: Allergic Reaction Warning for Pfizer/BioNTech Vaccine](#) - Medscape - Dec 09, 2020.
8. CDC MMWR. [ACIP Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine — United States](#), December 13, 2020.
9. ACIP Clinical Considerations: <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-12/slides-12-12/COVID-03-Mbaeyi.pdf>
10. US Centers for Disease Control and Prevention. Vaccines & Immunizations. [Understanding and Explaining mRNA COVID-19 Vaccines](#).