Emergency Use Authorization

Overview and Considerations for COVID-19 Vaccines

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Introduction

- The COVID-19 pandemic continues in the U.S. and world-wide
  - >28 million cases, >500,000 deaths in U.S. to date*
  - >400,000 new cases, >2,000 deaths in U.S. in the week ending February 24, 2021*
- On December 11, 2020, FDA issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine, for prevention of COVID-19 disease due to SARS-CoV-2 in individuals 16 years of age and older
- On December 18, 2020, and EUA was issued for the Moderna COVID-19 vaccine for prevention of COVID-19 disease in individuals 18 years of age and older
- Both of these COVID-19 vaccines remain unapproved products and are not available in sufficient quantities to address public health needs; thus, there is no adequate, approved, and available alternative in the US for prevention of COVID-19

*Centers for Disease Control and Prevention, https://covid.cdc.gov/covid-data-tracker/

Janssen's EUA Request

- On February 4, 2021, Janssen Biotech, Inc. submitted an EUA request for their COVID-19 Ad26-based vaccine (Ad26.COV2.S)
  - Ad26.COV2.S vaccine administered as a 1 dose regimen
  - Requested use is for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older
  - Information submitted with the request includes safety and efficacy data from a large (N>43,000) randomized, blinded, placebo-controlled Phase 3 trial COV3001 (ENSEMBLE)
  - Participants were enrolled from 8 countries: United States, Argentina, Brazil, Chile, Colombia, Mexico, Peru and South Africa

FDA Review of Janssen's EUA Request

- FDA has been conducting a comprehensive review of the Janssen COVID-19 vaccine EUA submission received on February 4, 2021, including:
  - Verification of clinical data integrity and Janssen's analyses, and additional FDA analyses, from datasets provided in the submission
  - Ongoing review of manufacturing, non-clinical, and clinical assay information
  - Review and revision of prescribing information and fact sheets for vaccine recipients and healthcare providers
  - Multiple information requests to Janssen to address questions and clarifications
  - Preparation for today's VRBPAC meeting
- Today's VRBPAC meeting continues FDA's commitment to an expedited review process that is transparent, scientifically sound, and data-driven

EUA Legal Authority

- Established in Section 564 of the Federal Food, Drug, and Cosmetic Act
- Allows for FDA authorization of unapproved medical products (or unapproved uses of approved medical products) to address public health emergencies related to biological, chemical, radiological, or nuclear agents
- Requires prior determination of a threat, and declaration of circumstances justifying need for EUA to address that threat, by the Secretary of Homeland Security, Defense, or Health and Human Services
  - HHS Secretary issued a declaration on March 27, 2020, justifying EUA of drugs and biological products to address the COVID-19 pandemic

Criteria for FDA Issuance of EUA

- The agent referred to in the EUA declaration can cause a serious or life-threatening disease or condition
- The known and potential benefits of the product outweigh the known and potential risks of the product
- No adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition

  – The Pfizer-BioNTech COVID-19 and Moderna vaccines are available under EUA for prevention of COVID-19 but remain unapproved (and quantity available for mass vaccination is limited)

COVID-19 Vaccine EUA - FDA Expectations

- FDA expectations were discussed in detail at October 22, 2020, and December 10 & 17, 2020, VRBPAC meetings and described in FDA Guidance, **Emergency Use Authorization for Vaccines to Prevent COVID-19**
  - Data to demonstrate manufacturing quality and consistency
  - Clear and compelling safety and efficacy data to support favorable benefit-risk of the vaccine when rapidly deployed for administration to millions of individuals, including healthy people
  - Plans for further evaluation of vaccine safety and effectiveness, including in ongoing clinical trials, active and passive safety monitoring during use under EUA, and observational studies

Issuance of EUA for a COVID-19 Vaccine

- Will specify conditions of use for which benefit-risk has been determined to be favorable based on review of available data
- Will provide information to vaccine recipients and healthcare providers by way of prescribing information and fact sheets
- EUA may be revised or revoked if other circumstances arise that warrant changes necessary to protect public health or safety, e.g. based on new information

VRBPAC Agenda

- Epidemiology of COVID-19 Variants and Postmarketing Surveillance from currently authorized COVID-19 vaccines- (CDC and FDA)
- 11AM Break (10 minutes)
- Sponsor Presentation (Janssen)
- Lunch break (30 minutes)
- Open Public Hearing
- FDA presentation and Voting Question
- Committee Discussion and Voting

Question for VRBPAC Vote (yes/no)

Based on the totality of scientific evidence available, do the benefits of the Janssen COVID-19 Vaccine outweigh its risks for use in individuals 18 years of age and older?


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FDA Expectations for Clinical Data

- Efficacy data from at least one well-designed Phase 3 trial demonstrating protection against SARS-CoV-2 infection or disease:
  - Point estimate of least 50% vs. placebo comparator
  - Appropriately alpha-adjusted confidence interval lower bound >30%
- Safety data from throughout clinical development to evaluate reactogenicity, serious AEs, and AEs of special interest
  - Including a high proportion of Phase 3 study subjects followed for at least 1 month after completion of the full vaccination regimen
- Sufficient cases of severe COVID-19 to assess for signals of enhanced disease (and preliminary evidence of protection against severe disease)

FDA Expectations for Clinical Data

- A planned case-driven interim efficacy analysis and associated safety analyses could provide data to support an EUA
  - These analyses should include a median follow-up duration of at least 2 months after completion of the full vaccination regimen
- Reasons for expectation of 2 months median follow-up:
  - Allows time for potential immune-mediated adverse reactions to be evaluated (uncommon but clinically significant immune-mediated adverse reactions to preventive vaccines generally have onset within 6 weeks following vaccination)
  - Ensures that vaccine efficacy is assessed during the time when adaptive/memory immune responses (rather than innate responses) are mediating protection
  - Allows for early assessment of waning protection and signals of enhanced disease

FDA Expectations for Further Evaluation

- Following issuance of an EUA, further vaccine evaluation would be needed:
  - For ongoing benefit/risk assessment to support continuation of the EUA
  - To accrue additional data to support licensure as soon as possible and/or to inform labeling
- Further vaccine evaluation following issuance of an EUA would include:
  - Longer-term follow-up for safety, including in larger numbers of vaccine recipients and in populations with lower representation in clinical trials
  - More precise estimation of vaccine effectiveness in specific populations
  - More robust assessment of effectiveness against aspects of SARS-CoV-2 infection or disease
  - Characterization of duration of protection
  - Assessment of effectiveness against relevant circulating strains
  - Investigation of immune biomarkers that might predict protection
  - Ongoing monitoring for signals of enhanced disease

FDA Expectations for Further Evaluation

- Issuance of an EUA for a COVID-19 vaccine would be contingent upon the ability to conduct further vaccine evaluation through a combination of:
  - Active follow-up of vaccine recipients under the EUA
  - Passive monitoring for clinically significant adverse reactions using established reporting mechanisms (e.g., VAERS)
  - Observational studies, including those that leverage healthcare claims databases
  - Continuation of blinded, placebo-controlled follow-up in ongoing clinical trials for as long as is feasible and strategies to handle loss of follow-up
  - Trial participants may choose to withdraw from follow-up for any reason, including to receive vaccine made available under EUA

COVID-19 Vaccines under EUA

- The mRNA-based BNT162b2 vaccine from Pfizer and BioNTech is authorized under an EUA for active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age, administered as 2 doses 3 weeks apart. Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE for the first primary endpoint against confirmed COVID-19 occurring at least 7 days after the 2nd dose was 95.0%

- The mRNA-1273 vaccine from Moderna Inc is authorized for use under an EUA for active immunization to prevent COVID-19 caused by SARS-CoV-2 in adults ≥18 years of age. The vaccine is administered as 2 doses 4 weeks apart. Among participants without history of SARS-CoV-2, VE for the primary endpoint against symptomatic COVID-19 (confirmed by an adjudication committee) occurring at least 14 days after the 2nd dose was 94.1%

COVID-19 Vaccinations in the United States*

- Number of people receiving 1 or more doses
  - 44,544,969 (13% of the population)
- Number of people receiving 2 doses
  - 19,882,544 (6% of the population)
- Total Doses Administered
  - 65,032,083

*: https://covid.cdc.gov/covid-data-tracker/#vaccinations as of February 18, 2021