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FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age

Today, the U.S. Food and Drug Administration authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 to include children 5 through 11 years of age. The authorization was based on the FDA's thorough and transparent evaluation of the data that included input from independent advisory committee experts who overwhelmingly voted in favor of making the vaccine available to children in this age group.

Key points for parents and caregivers:

Effectiveness: Immune responses of children 5 through 11 years of age were comparable to those of individuals 16 through 25 years of age. In addition, the vaccine was found to be 90.7% effective in preventing COVID-19 in children 5 through 11.

Safety: The vaccine's safety was studied in approximately 3,100 children age 5 through 11 who received the vaccine and no serious side effects have been detected in the ongoing study.

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices will meet next week to discuss further clinical recommendations.

"As a mother and a physician, I know that parents, caregivers, school staff, and children have been waiting for today's authorization. Vaccinating younger children against COVID-19 will bring us closer to returning to a sense of normalcy," said Acting FDA Commissioner Janet Woodcock, M.D. "Our comprehensive and rigorous evaluation of the data pertaining to the vaccine's safety and effectiveness should help assure parents and guardians that this vaccine meets our high standards."

The Pfizer-BioNTech COVID-19 Vaccine for children 5 through 11 years of age is administered as a two-dose primary series, 3 weeks apart, but is a lower dose (10 micrograms) than that used for individuals 12 years of age and older (30 micrograms).

In the U.S., COVID-19 cases in children 5 through 11 years of age make up 39% of cases in individuals younger than 18 years of age. According to the CDC, approximately 8,300 COVID-19 cases in children 5 through 11 years of age resulted in hospitalization. As of Oct. 17, 691 deaths from COVID-19 have been reported in the U.S. in individuals less than 18 years of age, with 146 deaths in the 5 through 11 years age group.

"The FDA is committed to making decisions that are guided by science that the public and healthcare community can trust. We are confident in the safety, effectiveness and manufacturing data behind this authorization. As part of our commitment to transparency around our decision-making, which included our public advisory committee meeting earlier this week, we have posted documents today supporting our decision and additional information detailing our evaluation of the data will be posted soon. We hope this information helps build confidence of parents who are deciding whether to have their children vaccinated," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research.

The FDA has determined this Pfizer vaccine has met the criteria for emergency use authorization. Based on the totality of scientific evidence available, the known and potential benefits of the Pfizer-BioNTech COVID-19 vaccine in individuals down to 5 years of age outweigh the known and potential risks.

FDA Evaluation of Available Effectiveness Data

The effectiveness data to support the EUA in children down to 5 years of age is based on an ongoing randomized, placebo-controlled study that has enrolled approximately 4,700 children 5 through 11 years of age. The study is being conducted in the U.S., Finland, Poland and Spain. Children in the vaccine group received two doses of the Pfizer-BioNTech COVID-19 Vaccine containing 10 micrograms of messenger RNA per dose. The FDA analyzed data that compared the immune response of 264 participants from this study to 253 participants 16 through 25 years of age who had two higher doses of the vaccine in a previous study which determined the vaccine to be effective in preventing COVID-19. The immune responses of the younger age participants were comparable to the older participants.

The FDA also conducted a preliminary analysis of cases of COVID-19 occurring seven days after the second dose. In this analysis, among participants without evidence of prior infection with SARS-CoV-2, 3 cases of COVID-19 occurred among 1,305 vaccine recipients and 16 cases of COVID-19 occurred among 663 placebo recipients; the vaccine was 90.7% effective in preventing COVID-19.

FDA Evaluation of Available Safety Data

The available safety data to support the EUA include more than 4,600 participants (3,100 vaccine, 1,538 placebo) ages 5 through 11 years enrolled in the ongoing study. In this trial, a total of 1,444 vaccine recipients were followed for safety for at least 2 months after the second dose.

Commonly reported side effects in the clinical trial included injection site pain (sore arm), redness and swelling, fatigue, headache, muscle and/or joint pain, chills, fever, swollen lymph nodes, nausea and decreased appetite. More children reported side effects after the second dose than after the first dose. Side effects were generally mild to moderate in severity and occurred within two days after vaccination, and most went away within one to two days.

The FDA and CDC safety surveillance systems have previously identified increased risks of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of tissue surrounding the heart) following vaccination with Pfizer-BioNTech COVID-19 Vaccine, particularly following the second dose, and with the observed risk highest in males 12 through 17 years of age. Therefore, the FDA conducted its own benefit-risk assessment using modelling to predict how many symptomatic COVID-19 cases, hospitalizations, intensive care unit (ICU) admissions and deaths from COVID-19 the vaccine in children 5 through 11 years of age would prevent versus the number of potential myocarditis cases, hospitalizations, ICU admissions and deaths that the vaccine might cause. The FDA's model predicts that overall, the benefits of the vaccine would outweigh its risks in children 5 through 11 years of age.

Ongoing Safety Monitoring

Pfizer Inc. has updated its safety monitoring plan to include evaluation of myocarditis, pericarditis and other events of interest in children 5 through 11 years of age. In addition, the FDA and the CDC have several systems in place to continually monitor COVID-19 vaccine safety and allow for the rapid detection and investigation of potential safety problems.

It is mandatory for Pfizer Inc. and vaccination providers to report to any serious adverse events, cases of Multisystem Inflammatory Syndrome and cases of COVID-19 that result in hospitalization or death in vaccinated individuals. It is also mandatory for vaccination providers to report all vaccine administration errors to VAERS for which they become aware and for Pfizer Inc. to include a summary and analysis of all identified vaccine administration errors in monthly safety reports to the FDA.

Data Supports New Vaccine Formulation to Improve Stability and Storage Conditions

The FDA today also authorized a manufacturing change for the vaccine to include a formulation that uses a different buffer; buffers help maintain a vaccine's pH (a measure of how acidic or alkaline a solution is) and stability. This new formulation is more stable at refrigerated temperatures for longer periods of time, permitting greater flexibility for vaccination providers.

The new formulation of the vaccine developed by Pfizer Inc. contains Tris buffer, a commonly used buffer in a variety of other FDA-approved vaccines and other biologics, including products for use in children. The FDA evaluated manufacturing data to support the use of Pfizer-BioNTech COVID-19 Vaccine containing Tris buffer and concluded it does not present safety or effectiveness concerns.

FDA News released Oct 29, 2021. www.fda.gov.

FDA Approves New Imaging Drug to Help Identify Ovarian Cancer Lesions

The U.S. Food and Drug Administration today approved Cytalux (pafolacianine), an imaging drug intended to assist surgeons in identifying ovarian cancer lesions. The drug is designed to improve the ability to locate additional ovarian cancerous tissue that is normally difficult to detect during surgery.

Cytalux is indicated for use in adult patients with ovarian cancer to help identify cancerous lesions during surgery. The drug is a diagnostic agent that is administered in the form of an intravenous injection prior to surgery.

"The FDA's approval of Cytalux can help enhance the ability of surgeons to identify deadly ovarian tumors that may otherwise go undetected," said Alex Gorovets, M.D., deputy director of the Office of Specialty Medicine in the FDA's Center for Drug Evaluation and Research. "By supplementing current methods of detecting ovarian cancer during surgery, Cytalux offers health care professionals an additional imaging approach for patients with ovarian cancer."

The American Cancer Society estimates there will be more than 21,000 new cases of ovarian cancer and more than 13,000 deaths from this disease in 2021, making it the deadliest of all female reproductive system cancers. Conventional treatment for ovarian cancer includes surgery to

remove as many of the tumors as possible, chemotherapy to stop the growth of malignant cells or other targeted therapy to identify and attack specific cancer cells.

Ovarian cancer often causes the body to overproduce a specific protein in cell membranes called a folate receptor. Following administration via injection, Cytalux binds to these proteins and illuminates under fluorescent light, boosting surgeons' ability to identify the cancerous tissue. Currently, surgeons rely on preoperative imaging, visual inspection of tumors under normal light or examination by touch to identify cancer lesions. Cytalux is used with a Near-Infrared fluorescence imaging system cleared by the FDA for specific use with pafolacianine.

The safety and effectiveness of Cytalux was evaluated in a randomized, multi-center, open-label study of women diagnosed with ovarian cancer or with high clinical suspicion of ovarian cancer who were scheduled to undergo surgery. Of the 134 women (ages 33 to 81 years) who received a dose of Cytalux and were evaluated under both normal and fluorescent light during surgery, 26.9% had at least one cancerous lesion detected that was not observed by standard visual or tactile inspection.

The most common side effects of Cytalux were infusion-related reactions, including nausea, vomiting, abdominal pain, flushing, dyspepsia, chest discomfort, itching and hypersensitivity. Cytalux may cause fetal harm when administered to a pregnant woman. The use of folate, folic acid, or folate-containing supplements should be avoided within 48 hours before administration of Cytalux. There is a risk of image interpretation errors with the use of Cytalux to detect ovarian cancer during surgery, including false negatives and false positives.

The FDA previously granted Cytalux orphan-drug, priority and fast track designations.

The FDA granted the approval to On Target Laboratories, LLC.

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FDA Approves First Drug to Prevent Graft Versus Host Disease

Today, the U.S. Food and Drug Administration approved Orencia (abatacept) for the prophylaxis (prevention) of acute graft versus host disease (aGVHD), a condition that occurs when donor bone marrow or stem cells attack the graft recipient, in combination with certain immunosuppressants. Orencia may be used in adults and pediatric patients two years of age or older undergoing hematopoietic stem cell transplantation (commonly known as bone marrow transplantation or stem cell transplantation) from an unrelated donor.

This is the first FDA drug approval for aGVHD prevention and incorporates real world evidence (RWE) as one component of the determination of clinical effectiveness. RWE is clinical evidence regarding the usage and potential benefits, or risks, of a medical product derived from analysis of real world data – i.e., data relating to patient health status and/or the delivery of health care routinely collected data from a variety of sources, including registry data. There are significant ongoing efforts at the FDA to incorporate use of high-quality RWE to support regulatory decision-making.

"Acute graft versus host disease can affect different parts of the body and become a serious post-transplant complication," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "By potentially preventing the disease, more patients may successfully undergo bone marrow or stem cell transplantation with fewer complications."

Acute GVHD is a potentially fatal complication that can occur after stem cell transplantation when the donor's immune cells (the graft) view the recipient's body (the host) as foreign, and the donated cells attack the body. The chances of developing aGVHD increase when the donor and recipient are not related or are not a perfect match.

The safety and efficacy of Orencia in combination with immunosuppressant therapy in patients age six years and older who underwent stem cell transplantation from a matched or mismatched unrelated donor were evaluated in two separate studies.

One study, GVHD-1, was a double-blind, placebo-controlled trial of 186 patients who underwent stem cell transplantation from a matched unrelated donor and randomly received Orencia or a placebo in combination with the immunosuppressive drugs. The study measured severe (grade III-IV) aGVHD-free survival, overall survival and moderate-severe (grade II-IV) aGVHD-free survival six months after transplantation. While severe aGVHD-survival was not significantly improved in patients who received Orencia (87%) compared to patients who received a placebo (75%), patients who received Orencia saw a

97% overall survival rate compared to 84% for patients who received a placebo. For moderate-severe aGVHD-free survival, patients who received Orencia saw a 50% rate compared to 32% for patients who received a placebo.

Additional evidence of effectiveness was provided by GVHD-2, a registry-based clinical study conducted using real world data from the Center for International Blood and Marrow Transplant Research in patients who underwent stem cell transplantation from a mismatched unrelated donor. This study analyzed outcomes of 54 patients treated with Orencia for the prevention of aGVHD, in combination with standard immunosuppressive drugs, versus 162 patients treated with standard immunosuppressive drugs alone. The study measured overall survival six months after transplantation. Patients who received Orencia saw a 98% overall survival rate compared to 75% for patients who received standard immunosuppression alone.

The most common side effects of Orencia for prevention of aGVHD include anemia, hypertension, cytomegalovirus (CMV) reactivation/CMV infection, fever, pneumonia, nosebleed, decreased levels of specific white blood cells called CD4 lymphocytes, increased levels of magnesium in the blood and acute kidney injury. Patients who receive Orencia should be monitored for Epstein-Barr virus reactivation in accordance with institutional practices and receive preventative medication for Epstein-Barr virus infection before starting treatment and for six months post-transplantation. Patients should also be monitored for CMV infection/reactivation for six months post-transplant.

Orencia received Breakthrough, Orphan Drug and Priority Review designations for this indication. Development of this product was partially supported by the FDA's Orphan Products Grants Program, which provides grants for clinical studies on safety and efficacy of products for use in rare diseases or conditions.

Orencia was originally approved by the FDA in 2005 for the treatment of adult rheumatoid arthritis. Orencia is also approved for the treatment of polyarticular juvenile idiopathic arthritis and adult psoriatic arthritis.

The FDA granted approval of Orencia to Bristol Myers Squibb.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, the FDA collaborated with Health Canada, Swissmedic and MOH (Israel's Ministry of Health). The application reviews are ongoing at the other regulatory agencies.

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Source: FDA