FDA Approves Vaccine for Use During Third Trimester of Pregnancy to Prevent Whooping Cough in Infants Younger Than Two Months of Age

Today, the U.S. Food and Drug Administration approved Boostrix (Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed [Tdap]) for immunization during the third trimester of pregnancy to prevent pertussis, commonly known as whooping cough, in infants younger than two months of age.

"Pertussis disease is a highly contagious respiratory illness affecting all age groups. However, babies are at highest risk for getting pertussis and having serious complications from it," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "While vaccination is the best method for providing protection, infants younger than two months of age are too young to be protected by the childhood pertussis vaccine series. This is the first vaccine approved specifically for use during pregnancy to prevent a disease in young infants whose mothers are vaccinated during pregnancy."

Pertussis is a common respiratory disease in the United States, resulting in frequent outbreaks. It is also called whooping cough because of the "whooping" sound that someone makes when gasping for air after a fit of coughing. Most serious pertussis cases, hospitalizations and deaths occur in infants younger than two months of age who are too young to be protected by the childhood pertussis vaccine series. According to the Centers for Disease Control and Prevention (CDC), 4.2% of the total cases of pertussis reported in the United States in 2021 were in infants younger than 6 months of age and approximately 31% required hospitalization. When the Boostrix vaccine is given during pregnancy, it boosts antibodies in the mother, which are transferred to the developing baby.

Boostrix was initially approved by the FDA in 2005 as a single dose for booster immunization against tetanus, diphtheria and pertussis in individuals 10 through 18 years of age. Subsequently, the FDA also approved Boostrix to include use in individuals 19 years of age and older and to include use of an additional dose 9 years or more after the initial dose of a Tdap vaccine. The FDA's approval of Boostrix has always included its use during pregnancy to protect the vaccinated individual. Today's approval is specific to use in pregnancy to prevent pertussis in infants younger than 2 months of age. Since 2012, the CDC has recommended the use of Tdap vaccines during the third trimester of each pregnancy.

The determination of effectiveness of Boostrix administered during the third trimester to prevent pertussis among infants younger than 2 months of age was based on a re-analysis of the Boostrix-relevant data from an observational case-control study of Tdap vaccine effectiveness. The FDA found these real-world data as providing real-world evidence to support this approval. In this re-analysis, data from 108 cases of pertussis in infants younger than 2 months of age (including four cases whose mothers received Boostrix during the third trimester) and 183 control infants who did not have pertussis (including 18 whose mothers received Boostrix during the third trimester) resulted in a preliminary estimate of Boostrix as 78% effective in preventing pertussis among infants younger than 2 months of age, when administered during the third trimester of pregnancy. This preliminary estimate of effectiveness was updated using data from published observational studies. These statistical analyses provided estimates of effectiveness that are consistent with the preliminary estimate of 78%.

The safety of Boostrix administered during the third trimester of pregnancy was assessed in a randomized, placebo-controlled study with a non-U.S. formulation of Boostrix. The FDA considers the safety data with the non-U.S. formulation relevant because it contains the same components as the U.S. formulation of Boostrix, except that the non-U.S. formulation contains more aluminum per dose. The study included approximately 680 pregnant individuals of whom about 340 received the non-U.S. formulation of Boostrix and of whom about 340 received saline placebo. After childbirth, the placebo recipients were then vaccinated with the non-U.S. formulation of Boostrix. The rates of reported side effects following receipt of the non-U.S. formulation of Boostrix administered during pregnancy were consistent with the rates following receipt of the non-U.S. formulation of Boostrix administered to study participants after childbirth.

The study did not identify any vaccine-related adverse effects on pregnancy or on the fetus/newborn.

In previous clinical studies, the most commonly reported side effects by individuals who received

Boostrix were pain, redness at the injection site, headache, fatigue and gastrointestinal symptoms.

Boostrix is administered as a single 0.5-mL dose.

The FDA granted the approval to GlaxoSmithKline Biologicals.

FDA News released Oct 7, 2022. www.fda.gov.

FDA Approves First Gene Therapy to Treat Adults with Hemophilia B

Today, the U.S. Food and Drug Administration approved Hemgenix (etranacogene dezaparvovec), an adeno-associated virus vector-based gene therapy for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

"Gene therapy for hemophilia has been on the horizon for more than two decades. Despite advancements in the treatment of hemophilia, the prevention and treatment of bleeding episodes can adversely impact individuals' quality of life," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "Today's approval provides a new treatment option for patients with Hemophilia B and represents important progress in the development of innovative therapies for those experiencing a high burden of disease associated with this form of hemophilia."

Hemophilia B is a genetic bleeding disorder resulting from missing or insufficient levels of blood clotting Factor IX, a protein needed to produce blood clots to stop bleeding. Symptoms can include prolonged or heavy bleeding after an injury, surgery, or dental procedure; in severe cases, bleeding episodes can occur spontaneously without a clear cause. Prolonged bleeding episodes can lead to serious complications, such as bleeding into joints, muscles or internal organs, including the brain. Most individuals who have Hemophilia B and experience symptoms are men. The prevalence of

Hemophilia B in the population is about one in 40,000; Hemophilia B represents about 15% of patients with hemophilia. Many women carriers of the disease have no symptoms. However, an estimated 10-25% of women carriers have mild symptoms; in rare cases, women may have moderate or severe symptoms.

Treatment typically involves replacing the missing or deficient clotting factor to improve the body's ability to stop bleeding and promote healing. Patients with severe Hemophilia B typically require a routine treatment regimen of intravenous (IV) infusions of Factor IX replacement products to maintain sufficient levels of clotting factor to prevent bleeding episodes.

Hemgenix is a one-time gene therapy product given as a single dose by IV infusion. Hemgenix consists of a viral vector carrying a gene for clotting Factor IX. The gene is expressed in the liver to produce Factor IX protein, to increase blood levels of Factor IX and thereby limit bleeding episodes.

The safety and effectiveness of Hemgenix were evaluated in two studies of 57 adult men 18 to 75 years of age with severe or moderately severe Hemophilia B. Effectiveness was established based on decreases in the men's annualized bleeding rate (ABR). In one study, which had 54 participants, the subjects had increases in Factor IX activity levels, a decreased need for routine Factor IX replacement prophylaxis, and a 54% reduction in ABR compared to baseline.

The most common adverse reactions associated with Hemgenix included liver enzyme elevations, headache, mild infusion-related reactions and flu-like symptoms. Patients should be monitored for adverse infusion reactions and liver enzyme elevations (transaminitis) in their blood.

This application received priority Review, Orphan and Breakthrough Therapy designations.

The FDA granted approval of Hemgenix to CSL Behring LLC.

FDA News released Nov 22, 2022. www.fda.gov.

FDA Approves New HIV Drug for Adults with Limited Treatment Options

Today, the U.S. Food and Drug Administration approved Sunlenca (lenacapavir), a new type of antiretroviral medication for adult patients living with human immunodeficiency virus type 1 (HIV-1), whose HIV infections cannot be successfully treated with other available treatments due to resistance, intolerance, or safety considerations. After the starting dose is completed, Sunlenca is administered as subcutaneous (under the skin) injections once every six months, allowing convenient dosing for patients.

"Today's approval ushers in a new class of antiretroviral drugs that may help patients with HIV who have run out of treatment options," said Debra Birnkrant, M.D., director of the Division of Antivirals in the FDA's Center for Drug Evaluation and Research. "The availability of new classes of antiretroviral medications may possibly help these patients live longer, healthier lives."

Sunlenca is the first of a new class of drugs called capsid inhibitors to be FDA-approved for treating HIV-1. Sunlenca works by blocking the HIV-1 virus' protein shell (the capsid), thereby interfering with multiple essential steps of the viral lifecycle. Sunlenca's starting dose is given as oral tablets and subcutaneous injections, followed by maintenance injections every six months; Sunlenca is given in combination with other antiretroviral(s).

The safety and efficacy of Sunlenca were established through a multicenter clinical trial with 72 patients whose HIV infections were resistant to multiple classes of HIV medications. These patients had to have high levels of virus in their blood despite being on antiretroviral drugs. Patients were enrolled into one of two study groups. One group was randomized to receive either Sunlenca or placebo in a double-blind fashion, and the other group received open-label Sunlenca. The primary measure of efficacy was the proportion of patients in the randomized study group who achieved a certain level of reduction in virus during the initial 14 days compared to baseline. In this group, 87.5% of patients who received Sunlenca achieved such a decrease in virus compared to 16.7% of patients who received a placebo. After 26 weeks of Sunlenca plus other antiretrovial drugs, 81% of participants in the first group achieved HIV RNA suppression, where levels of HIV were low enough to be considered undetectable. After 52 weeks, 83% of participants continued to have HIV RNA suppression.

The most common adverse reactions with Sunlenca were injection site reactions and nausea. Most injection site reactions were described as swelling, pain or redness. Sunlenca comes with certain warnings and precautions. Injection site reactions described as nodules or indurations may be persistent in some patients. Additional warnings and precautions include the risk of developing immune reconstitution syndrome, which is when the immune system overreacts after starting HIV treatment. Also, small (residual) amounts of Sunlenca can remain in the body for up to a year or longer; low levels of drug caused by missing doses of Sunlenca or failing to maintain a fully suppressive HIV treatment regimen after stopping Sunlenca could lead to an increased risk of developing viral resistance. Residual amounts of Sunlenca could also lead to potential drug interactions.

Patients should not receive Sunlenca if they also take certain drugs that cause reduced levels of Sunlenca. This may result in losing virologic response and developing viral resistance.

The FDA granted Sunlenca Priority Review, Fast Track and Breakthrough Therapy designations for this indication.

The FDA granted the approval of Sunlenca to Gilead Sciences.

FDA News released Dec 22, 2022. www.fda.gov.

Source: FDA