National Vaccine Information Center

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Vaccines and Related Biological Products Advisory Committee
Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Via: Regulations.gov

Re: Docket No. FDA-2023-N-1338 for "Vaccines and Related Biological Products Advisory Committee (VRBPAC); Notice of Meeting; Establishment of a Public Docket; Request for Comments." Federal Register Citation 88 FR 24191 and 88 FR 6.

Dear Committee Members,

The National Vaccine Information Center (NVIC) provides the following as our public comment for the above referenced docket providing notice to the public of the VRBPAC's upcoming meeting to discuss and make recommendations of Pfizer's Abrysvo "for the prevention" of RSV in infants from birth through 6 months of age by through vaccination of pregnant individuals. We note that as of this writing the background materials for the upcoming meeting are not available to reference in our written public comment.

Respiratory Syncytial Virus (RSV) and Burden

RSV is a common respiratory infection with symptoms such as fever, runny nose, and cough, similar to the common cold. The majority of individuals experience uncomplicated cases and recover within a few days,[1] though some individuals will develop lower respiratory infections requiring medical attention and sometimes hospitalization.[2]

As reported by the U.S. Centers for Disease Control (CDC), it is estimated that the burden of disease for children under 5 years of age is 2.1 million non-hospitalized cases, and an additional 58,000 to 80,000 hospitalized cases.[3] [4] Additionally, almost all children get RSV by the time they reach two years of age, with premature infants and immunocompromised children being at the highest risk for severe RSV disease.[5]

The study that the CDC relies upon for burden estimates also states that 78 percent of RSV infections for this age group occur in children over one year of age,[6] meaning that the subject population under consideration for potential protection via the vaccination of pregnant women is under 22 percent. The total disease burden in the U.S. is estimated to be about 4.1 million cases annually, with the remaining burden largely attributed to individuals 65 years of age and older.[7]

Vaccine Efficacy Prevention of RSV

Policy rationale used by public health officials for recommending pregnant women receive RSV vaccine is the theoretical passing on of protective antibodies to their unborn children to prevent RSV in infants from birth through six months of age.[8] However, CDC officials have stated as recently as February that:

> *"There is no established immunologic correlate of protection for RSV."*[9]

During the February meeting of the CDC's Advisory Committee on Immunization Practices (ACIP), Pfizer reported RSV vaccine efficacy in primary endpoints for infants as 57.1 percent at 90 days after birth, waning to 51.3 percent at 180 days and 41 percent at 360 days. Vaccine efficacy for severe RSV was reported at 81.8 percent at 90 days after birth, waning to 69.4 percent at 180 days. Vaccine efficacy related to hospitalizations was reported to be 67.7 percent at 90 days after birth, waning to 33.3 percent at 360 days.[10]

NVIC believes that the federal government should also make available to the public estimates of absolute risk reduction (ARR) for all outcomes reported by Pfizer. In an attempt to produce ARR estimates, NVIC used the University of Illinois online Risk Reduction Calculator and found that the vaccine appears to provide an absolute risk reduction of only about 1.7[11] [12] percent for severe RSV infections and about 1.2[13] [14] percent for medically attended RSV illnesses from birth to 180 days,[15] with numbers needed to vaccinate (NNV) to prevent one case of at 129[16] and 81[17] individuals, respectively. These estimates need to be confirmed by FDA and CDC. ARR using the same calculator related to hospitalizations reported by Pfizer was less than one percent at 180 days after birth, with NNV at 139 individuals to prevent one case of hospitalization.[18] [19]

Of concern is that data presented by the CDC during the ACIP demonstrating that Abrysvo doesn't prevent transmission of RSV in adults age 60 and older, putting into question the prevention of transmission in infants.

Vaccine Cost Effectiveness

While a cost analysis relating to the use of RSV vaccine during pregnancy is not yet available, such an analysis was presented to the ACIP in February for adults. The analysis demonstrated that Pfizer's Abrysvo RSV vaccine was not cost-effective in reducing the burden of costs associated with RSV illness in adults aged 65 and older.[20]

This older population represents roughly half of the overall RSV illness burden in the U.S. Given this data, it would appear unlikely that the receipt of RSV vaccine in pregnant women will be cost-effective in the prevention of RSV illness in infants from birth to six months of age, which represents less than 22% of the overall burden.[21]

Vaccine Adverse Events in Pregnant Women and Babies in RSV Vaccine Clinical Trials

As with any pharmaceutical product, the Abrysvo RSV vaccine is not without risk to pregnant women and their unborn children. Pfizer clinical trial data for pregnant women reveals that nearly 14 percent experienced a vaccine adverse event, with 4.2 percent reported as serious, 1.7 percent reported as severe, and 0.5 percent as life-threatening.[22]

Additionally, 37.1 percent of infants born to RSV vaccinated pregnant women were reported to have experienced an adverse event within one month of birth. Of these reports, 15.5 percent were reported as serious, 4.5 percent as severe, and 1 percent as life-threatening.[23] Pfizer data also demonstrates that Abrysvo may increase the risk for premature birth, and low birth weight infants. The clinical trial

data also show that the vaccine may contribute to an increased risk for death in women and stillbirths, though Pfizer has stated these deaths are unrelated to the vaccine.[24]

Lastly, questions about whether the Abrysvo clinical trial was representative and the sample size was large enough to be sufficiently powered to detect differences in outcomes need to be addressed for the public. It appears that the Abrysvo trial may be underpowered and not representative of other risks to pregnant women, such as Guillain-Barré Syndrome (GBS). Pfizer's clinical data on pregnant women is based on 3,682 vaccinated participants.[25] Notably, Pfizer's February briefing documents submitted to the VRBPAC for Abrysvo stated that there were two cases of vaccine-related GBS among the 19,942 vaccinated participants enrolled in the clinical trial for adults 60 years of age and older, a rate that may put the risk of GBS as high as one in 10,000.[26]

Clinical Trial Data and Cost Analysis Do Not Support Approval

Given the above data, Abrysvo RSV vaccine represents an unnecessary risk to mother and child for very meager reductions in RSV cases, severe and typical, as well as hospitalizations, for an illness that represents little threat to healthy infants. Additionally, the clinical trial sample size appears to be underpowered and is not likely to capture severe vaccine adverse events, such as GBS. Data also suggest that even with the small sample size the vaccine may contribute to undesirable events such as premature birth and low birth weight in infants.

While the global market for RSV vaccine has been estimated to be over $10 billion by 2030,[27] it makes little fiscal sense for the government to expend monies for use of Abrysvo vaccine in pregnant women under the guise of providing protection for infants, particularly when there is no correlate of protection for RSV and trial data demonstrates the vaccine will not prevent the transmission of the illness.

For these reasons, NVIC opposes the use of Abrysvo in pregnant women and strongly encourages the VRBPAC and FDA to reject the use of Abrysvo in pregnant women.

Sincerely,

/s/ *Theresa Wrangham*

Theresa Wrangham,
Executive Director

References

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