FDA Approves Two-Dose Rotavirus Vaccine

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The Food and Drug Administration approved the Rotarix vaccine on April 3, making it the second vaccine approved for the treatment of rotavirus in the United States.

The oral live-attenuated vaccine, manufactured by GlaxoSmithKline Biologicals, is approved for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9) in infants and children when administered as a two-dose series between the ages of 6 and 24 weeks, according to the FDA statement announcing the approval. Rotarix—previously approved in more than 100 countries, where more than 25 million doses have been distributed—will be available commercially in the United States in the second half of 2008, according to GSK.

Approval was based on the results of studies of more than 24,000 infants worldwide, which found that Rotarix was effective in preventing mild and severe cases of gastroenteritis caused by rotavirus during the first 2 years of life, the FDA said. Fussiness and irritability, cough and runny nose, fever, loss of appetite, and vomiting were the most common adverse events reported during the trials.

A study of more than 63,000 infants in Latin America and Finland, conducted by GSK to assess the risk of intussusception associated with Rotarix, found no increased risk among the 31,673 infants who received the vaccine, when compared with the 31,552 infants who received placebo.

An increased risk of intussusception led to the voluntary withdrawal of RotaShield—the first approved rotavirus vaccine—from the market in 1999. Rotateq, the live oral rotavirus vaccine manufactured by Merck & Co., was approved in February 2006; it is administered as a three-dose series to children between the ages of 6 and 32 weeks.

In the GSK intussusception study, however, the rates of pneumonia-related deaths and convulsions were higher among the vaccine recipients. The FDA has concluded that the available data "do not establish that these events are related to the vaccine," but has requested that the company conduct a postmarketing study in the United States of more than 40,000 infants to provide more data on the vaccine's safety.

The observational study will enroll approximately 44,000 Rotarix recipients in the United States and will evaluate the potential increased risk of intussusception, Kawasaki disease, hospitalizations caused by acute lower respiratory tract infections, and convulsions.

That request reflects the recommendations of the FDA's Vaccines and Related Biological Products Advisory Committee, which reviewed the vaccine's safety and efficacy at a meeting in February. At that meeting, the panel voted 12-0 that the available data adequately supported the efficacy of Rotarix for preventing rotavirus caused by the serotypes included in the vaccine (G1, G2, G3, G4, and G9), and voted 11 to 1 that the data adequately supported the vaccine's safety. The panel, however, recommended a postmarketing study to follow adverse events associated with the previous rotavirus vaccines, including intussusception and Kawasaki disease, and the new signal for pneumonia deaths and a higher rate of convulsions in the Rotarix studies.

GSK's proposed indication for the vaccine included protection from the G2 subtype, but at the meeting, advisory panel members expressed concern about the vaccine's efficacy against the G2 serotype and agreed this issue could be addressed in the vaccine's labeling. The G2 strain is not included in the approved indication, which is for protection against the G1, G3, G4, and G9 strains of rotavirus.

At the FDA meeting, GSK also presented data that found that coadministration of Rotarix did not have a negative effect on the immune responses to the antigens in Pediarix, Prevnar, and ActHIB.

"This vaccine provides another option to combat and reduce a potentially severe illness that affects so many children," Dr. Jesse Goodman, director of the FDA's Center for Biologics Evaluation and Research, said in the FDA statement.

Approximately 2.7 million cases of gastroenteritis in children in the United States every year are caused by rotavirus; about 55,000-70,000 of these children require hospitalization, and 20-60 deaths are caused by rotavirus, according to the FDA.