Update on Japanese Encephalitis Vaccine for Children --- United States, May 2011

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Inactivated mouse brain--derived Japanese encephalitis (JE) vaccine (JE-MB [manufactured as JE-Vax]), the only JE vaccine that is licensed for use in children in the United States, is no longer available. This notice provides updated information regarding options for obtaining JE vaccine for U.S. children.

JE among U.S. travelers

JE virus is the leading cause of vaccine-preventable encephalitis in Asia and the western Pacific. For most travelers to Asia, the risk for JE is low but varies on the basis of destination, duration, season, and activities. During the past 4 decades, 17 cases of JE have been reported among U.S. travelers and expatriates, including three cases among U.S. children aged <18 years (1,2). JE is a severe disease; 20%--30% of patients die, and 30%--50% of survivors have neurologic or psychiatric sequelae (3).

Recommendations for prevention of JE among travelers

The Advisory Committee on Immunization Practices (ACIP) recommends that all travelers, including children, take precautions to avoid mosquito bites to reduce the risk for JE and other vector-borne infectious diseases (3). These precautions include using insect repellent, permethrin-impregnated clothing, and bed nets, and staying in accommodations with screened or air-conditioned rooms. Additional information on protection against mosquitoes and other arthropods is available in CDC's *Health Information for International Travel* (Yellow Book) (*4*). For some travelers who will be in a high-risk setting on the basis of season, location, duration, and activities, JE vaccine can reduce the risk for disease further (3).

JE vaccine for U.S. children

JE-MB has been licensed in the United States since 1992 for use in adults and children aged ≥1 year. JE-MB has been associated with serious, but rare, allergic and neurologic adverse events (3). During 2002--2009, a total of 848,571 doses of JE-MB were distributed in the United States (mean: 106,071 doses per year), of which 534,330 (63%) doses were distributed to military health-care providers (*5*). During this period, an estimated 2,000--3,000 doses of JE-MB were distributed for use in U.S. children each year (Sanofi Pasteur, unpublished data, 2011). However, JE-MB is no longer being produced, and all remaining doses expire in May 2011.

In 2009, the Food and Drug Administration (FDA) approved an inactivated Vero cell culture-derived JE vaccine (JE-VC [manufactured as Ixiaro]) for use in adults aged ≥17 years. One pediatric dose-ranging study has been completed among 60 children aged 12--35 months in India (48 children received JE-VC, and 12 children received another inactivated mouse brain--derived JE vaccine [manufactured as JenceVac]) (*6*). A safety and immunogenicity study is ongoing among approximately 1,900 children aged 2 months--17 years in the Philippines, and a safety and immunogenicity bridging study has been initiated in the United States and other nonendemic countries with a targeted enrollment of approximately 100 children. Despite these ongoing studies, it likely will be several years before JE-VC is licensed in the United States for use in children. JE-VC product information is available online from FDA at http://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm179132.htm.

Current options for obtaining JE vaccine for U.S. children

For U.S. health-care providers interested in obtaining JE vaccine for pediatric patients they judge to be at risk, current options include 1) enroll children in the ongoing clinical trial, 2) administer JE-VC off-label, or 3) receive JE vaccine at an international travelers' health clinic in Asia.

The ongoing pediatric safety and immunogenicity trial with JE-VC is enrolling children aged 2 months--17 years at five U.S. sites (trial identifier NCT01047839). The study is open-label, and all enrollees receive 2 doses of JE-VC administered 28 days apart. A third study visit is required at 56 days after the first dose of vaccine. Additional information about the clinical trial is available online from the National Institutes of Health at http://clinicaltrials.gov/ct2/show/nct01047839. In addition, a list of U.S. clinical trial sites and contact information is available online from CDC at http://www.cdc.gov/ncidod/dvbid/jencephalitis/children.htm.

JE-VC is FDA-licensed for use in adults aged ≥17 years. However, a health-care provider may choose to administer the vaccine off-label in children aged <17 years. Data from the one completed pediatric study have been published (*6*). Additional information about the use of JE-VC in children is available from Novartis Medical Communications by telephone (877-683-4732) or e-mail (vaccineinfo.us@novartis.com).

Several JE vaccines are manufactured and available for pediatric use in Asia but are not licensed in the United States. Vaccines available at international travelers' health clinics in Asia include another inactivated mouse brain--derived JE vaccine manufactured in South Korea, live attenuated SA 14-14-2 vaccine manufactured in China, or another Vero cell culture-derived JE vaccine manufactured in Japan. The recommended number of doses and schedule varies by vaccine and country. A partial list of international travelers' health clinics in Asia that administer JE vaccines to children is available online from CDC at http://www.cdc.gov/ncidod/dvbid/jencephalitis/children.htm.

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