Licensure of a Haemophilus influenzae Type b (Hib) Vaccine (Hiberix) and Updated Recommendations for Use of Hib Vaccine

Weekly

September 18, 2009 / 58(36);1008-1009

On August 19, 2009, the Food and Drug Administration (FDA) licensed Hiberix (GlaxoSmithKline Biologicals, Rixensart, Belgium), a *Haemophilus influenzae* type b (Hib) conjugate vaccine composed of *H. influenzae* type b capsular polysaccharide (polyribosyl-ribitol-phosphate [PRP]) conjugated to inactivated tetanus toxoid (PRP-T). Hiberix is licensed for use as the booster (final) dose of the Hib vaccine series for children aged 15 months through 4 years (before the 5th birthday) who have received previously the primary series of Hib vaccination (consisting of 2 or 3 doses, depending on the formulation) (*1*). The Advisory Committee on Immunization Practices (ACIP) recommends Hib booster vaccination for children at ages 12 through 15 months; however, because of the recent shortage of Hib vaccines, many children have deferred the booster dose and therefore require catch-up vaccination (*2*). This report summarizes the indications for Hiberix use and provides guidance on Hib booster dose administration based on increasing vaccine supplies. Vaccination recommendations in this report update the previous advisory on Hib booster administration (June 26, 2009) (*2*), which advised that children with deferred booster doses receive it at the next regularly scheduled visit. Vaccination providers are now recommended to begin recall of children in need of the booster dose when feasible and monovalent Hib vaccine supply in the office is adequate.

Hiberix Licensure

FDA licensed the new vaccine after review of safety and immunogenicity data from seven core studies conducted outside the United States that evaluated Hiberix for the booster dose in 1,008 children (*3,4*). The children in these studies received various Hib conjugate vaccines for the primary series, including Hiberix (not approved for primary series in the United States), and the monovalent Hib vaccines currently licensed for primary series in the United States, ActHIB (PRP-T, Sanofi Pasteur, Swiftwater, Pennsylvania) and PedvaxHIB (PRP-OMP, Merck & Co., Inc., West Point, Pennsylvania). In the seven core studies, Hiberix was given concomitantly with one of the following vaccines (all non-U.S. formulations, not licensed in the United States; GlaxoSmithKline Biologicals): diphtheria, tetanus, and acellular pertussis vaccine (DTaP), DTaP-hepatitis B vaccine (DTaP-HBV), DTaP-HBV-inactivated polio vaccine (DTaP-HBV-IPV), or DTaP-inactivated polio vaccine (DTaP-IPV). Serologic endpoints showed that the booster dose of Hiberix provided levels of antibodies protective against Hib invasive disease. Rates of adverse events generally were comparable to those observed with other childhood vaccines. In one of the core studies with 371 children, the frequencies of solicited local symptoms (i.e., redness, pain, or swelling) were each less than 25% (*3*), comparable to that reported in studies of currently licensed monovalent Hib conjugate vaccines (*1*). Hiberix was first introduced to markets outside the

United States in 1996 and is used in nearly 100 countries (*3,4*).

Hiberix is supplied as a lyophilized powder for reconstitution in sterile 0.9% saline solution (*3*). Each 0.5 mL intramuscular dose of Hiberix contains 10 μg of purified *H. influenzae* type b capsular polysaccharide (polyribosyl-ribitol-phosphate [PRP]) conjugated to inactivated tetanus toxoid (PRP-T) (*3*). Hiberix does not contain thimerosal (*3*).

Indications and Guidance for Use

Hiberix is licensed for use as the booster (final) dose for Hib vaccination for children aged 15 months through 4 years (before the 5th birthday) who have received a primary Hib vaccination series of 2 or 3 doses (depending on the formulation of the primary series vaccines). ACIP recommends Hib booster dosing at ages 12 through 15 months (*1*). To facilitate timely booster vaccination, Hiberix and other Hib conjugate vaccines can be administered as early as age 12 months, in accordance with Hib vaccination schedules for routine and catch-up immunization (*5*). Hiberix is not licensed for the primary Hib vaccination series; however, if Hiberix is administered inadvertently during the primary vaccination series, the dose should be counted as a valid PRP-T dose that does not need to be repeated if it was administered according to schedule (*5*). In these children, a total of 3 doses will complete the routine primary series.

Children aged 12 months through 4 years (before the fifth birthday) who did not receive a booster because of the recent shortage of Hib vaccines should receive a booster with any of the available Hib-containing vaccines at the earliest opportunity (*2*). With licensure of Hiberix and anticipated distribution, the increased supply of Hib-containing vaccines will be sufficient to support a provider-initiated notification process to contact all children whose Hib booster dose had been deferred. When feasible and when vaccine supply in the office is sufficient, vaccination providers should review electronic or paper medical records or immunization information system (e.g., registry) records to identify and recall children in need of a booster dose. If supplies are not adequate, providers should continue to follow previous recommendations to provide the booster dose at the child's next regularly scheduled visit (*2*).

Information Regarding Supply of Hiberix, ActHib, and Pentacel

At this time, production of Merck Hib vaccine products remains suspended; however, supplies of Sanofi Pasteur vaccines ActHIB (monovalent Hib vaccine) and Pentacel (DTaP-IPV/Hib) are available for use for the primary Hib vaccination series and booster in infants and children. Vaccination providers with questions about supplies of Hiberix monovalent Hib vaccine purchased with nonpublic funds should contact GlaxoSmithKline Biologicals' customer service department (telephone, 866-475-8222). Providers with questions about supplies of ActHIB or Pentacel purchased with nonpublic funds should contact Sanofi Pasteur's customer service department (telephone, 800-822-2463). For public vaccine supplies, including Vaccines for Children Program vaccine, providers should contact their state/local immunization program to obtain vaccine. Providers ordering Hiberix through the Vaccines for Children Program may place orders in early October.

This recommendation reflects CDC's assessment of the existing national Hib vaccine supply and will be updated if the supply changes. Updated information about the national Hib vaccine supply is available at http://www.cdc.gov/vaccines/vac-gen/shortages/default.htm. Details about the routine Hib vaccination schedule are available at http://www.cdc.gov/vaccines/recs/schedules/default.htm#child. Adverse events after receipt of any vaccine should be reported to the Vaccine Adverse Event Reporting System at http://vaers.hhs.gov.

References

**Questions or messages regarding errors in formatting should be addressed to mmwrq@cdc.gov.

Date last reviewed: 9/17/2009