

# Notice to Readers: FDA Approval for a Combined Hepatitis A and B Vaccine



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On May 11, 2001, the Food and Drug Administration (FDA) licensed a combined hepatitis A and B vaccine (Twinrix<sup>®</sup>) for use in persons aged  $\geq 18$  years. Twinrix is manufactured and distributed by GlaxoSmithKline Biologicals (Rixensart, Belgium), and is made of the antigenic components used in Havrix and Engerix-B (GlaxoSmithKline). The antigenic components in Twinrix have been used routinely in separate single antigen vaccines in the United States since 1995 and 1989 as hepatitis A and B vaccines, respectively.

## Vaccine Description

Each dose of Twinrix contains at least 720 enzyme-linked immunosorbent assays units of inactivated hepatitis A virus and 20 mcg of recombinant hepatitis B surface antigen (HBsAg) protein, with 0.45 mg of aluminum in the form of aluminum hydroxide and aluminum phosphate as adjuvants, 5.0 mg 2-phenoxyethanol as a preservative, and pH stabilizer in normal saline. Trace amounts of thimerosal ( $<1 \mu\text{g}$  mercury), neomycin ( $\leq 20$  ng), formalin ( $\leq 0.1$  mg), and yeast protein ( $\leq 5\%$ ) also are present from the manufacturing process.

## Indications and Usage

Twinrix is indicated for vaccination of persons aged  $\geq 18$  years against hepatitis A and B. Any person in this age group having an indication for both hepatitis A and B vaccination can be administered Twinrix, including patients with chronic liver disease, users of illicit injectable drugs, men who have sex with men, and persons with clotting factor disorders who receive therapeutic blood products (1,2). For international travel, hepatitis A vaccine is recommended for travelers to areas of high or intermediate hepatitis A endemicity; hepatitis B vaccine is recommended for travelers to areas of high or intermediate hepatitis B endemicity who plan to stay for  $\geq 6$  months and have frequent close contact with the local population (3). Primary vaccination consists of three doses, given on a 0-, 1-, and 6-month schedule, the same schedule as that used for single antigen hepatitis B vaccine.

## Safety and Immunogenicity

Adverse experiences (AEs) were evaluated in clinical trials in which 6594 doses of Twinrix were administered to 2165 persons. Observed AEs generally were similar in type and frequency to those observed after vaccination with monovalent hepatitis A and B vaccines. The frequency of AEs did not increase with subsequent doses of Twinrix. No serious vaccine-related AEs were observed (GlaxoSmithKline Biologicals,

unpublished data, 2001). Twinrix is contraindicated in persons with known hypersensitivity to any component of the vaccine.

Preliminary clinical trials indicate that the immunogenicity of Twinrix is equivalent to that of the single antigen hepatitis vaccines. Data from 11 clinical trials that included adults aged 17--70 years indicated, 1 month after completion of the three dose series, seroconversion for antibodies against hepatitis A virus (anti-HAV titer  $\geq 20$  mIU/mL or 33mIU/mL [Enzygum-Test, Boehringer Mannheim Immunodiagnostics, Mannheim, Germany]) were elicited in 99.9% of vaccinees, and protective antibodies against HBsAg (anti-HBs  $\geq 10$  mIU/mL [AUSAB, Abbott Laboratories, Abbott Park, Illinois]) were elicited in 98.5% of vaccinees. One month after one dose of Twinrix, seroconversion to anti-HAV was seen in 93.8% of vaccinees and protective anti-HBs concentrations in 30.8%. One month after the second dose, seroconversion to anti-HAV was seen in 98.8% of vaccinees, and protective anti-HBs concentrations in 78.2%. The efficacy of Twinrix is expected to be comparable with existing single antigen hepatitis vaccines. The persistence of anti-HAV and anti-HBs following Twinrix administration is similar to that following single antigen hepatitis A and B vaccine administration at 4 years follow-up (GlaxoSmithKline Biologicals, unpublished data, 2001). Additional information is available from the manufacturer's package insert and GlaxoSmithKline Vaccines, telephone (800) 366-8900.

## References

1. CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1999;48(no. RR-12).
2. CDC. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1991;40(no. RR-13).
3. CDC. Health information for international travel 2001--2002. Atlanta, Georgia: US Department of Health and Human Services, Public Health Service, CDC, 2001.

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