PRESCRIBING INFORMATION

HAVRIX®

(Hepatitis A Vaccine, Inactivated)

DESCRIPTION

HAVRIX (Hepatitis A Vaccine, Inactivated) is a noninfectious hepatitis A vaccine developed and manufactured by GlaxoSmithKline Biologicals. The virus (strain HM175) is propagated in MRC-5 human diploid cells. After removal of the cell culture medium, the cells are lysed to form a suspension. This suspension is purified through ultrafiltration and gel permeation chromatography procedures. Treatment of this lysate with formalin ensures viral inactivation. HAVRIX contains a sterile suspension of inactivated virus; viral antigen activity is referenced to a standard using an enzyme linked immunosorbent assay (ELISA), and is therefore expressed in terms of ELISA Units (EL.U.).

HAVRIX is supplied as a sterile suspension for intramuscular administration. The vaccine is ready for use without reconstitution; it must be shaken before administration since a fine white deposit with a clear colorless supernatant may form on storage. After shaking, the vaccine is a slightly turbid white suspension.

Each 1-mL adult dose of vaccine consists of 1440 EL.U. of viral antigen, adsorbed on 0.5 mg of aluminum as aluminum hydroxide.

Each 0.5-mL pediatric dose of vaccine consists of 720 EL.U. of viral antigen, adsorbed onto 0.25 mg of aluminum as aluminum hydroxide.

Excipients are: Amino acid supplement (0.3% w/v) in a phosphate-buffered saline solution and polysorbate 20 (0.05 mg/mL). Residual MRC-5 cellular proteins (not more than 5 mcg/mL) and traces of formalin (not more than 0.1 mg/mL) are present. Neomycin sulfate, an aminoglycoside antibiotic, is included in the cell growth media; only trace amounts (not more than 40 ng/mL) remain following purification.

HAVRIX is formulated without preservatives.

CLINICAL PHARMACOLOGY

The hepatitis A virus (HAV) belongs to the picornavirus family. It is one of several hepatitis viruses that cause systemic disease with pathology in the liver.

The incubation period for hepatitis A averages 28 days (range: 15 to 50 days).[1] The course of hepatitis A infection is extremely variable, ranging from asymptomatic infection to icteric hepatitis and death.[2]

The presence of antibodies to HAV (anti-HAV) confers protection against hepatitis A infection. However, the lowest titer needed to confer protection has not been determined.

Protective Efficacy: Protective efficacy with HAVRIX has been demonstrated in a double-blind, randomized controlled study in school children (age 1 to 16 years) in Thailand who were at high risk of HAV infection. A total of 40,119 children were randomized to be vaccinated with either HAVRIX 360 EL.U. or ENGERIX-B® [Hepatitis B Vaccine (Recombinant)] at 0, 1,

and 12 months. 19,037 children received a primary course (doses at 0 and 1 months) of HAVRIX and 19,120 children received a primary course (doses at 0 and 1 months) of ENGERIX-B. 38,157 children entered surveillance at day 138 and were observed for an additional 8 months. Using the protocol-defined endpoint (≥2 days absence from school, ALT level >45 U/mL, and a positive result in the HAVAB-M test), 32 cases of clinical hepatitis A occurred in the control group. In the HAVRIX group, 2 cases were identified. These 2 cases were mild in terms of both biochemical and clinical indices of hepatitis A disease. Thus the calculated efficacy rate for prevention of clinical hepatitis A was 94% (95% confidence intervals 74% to 98%).[3]

In outbreak investigations occurring in the trial, 26 clinical cases of hepatitis A (of a total of 34 occurring in the trial) occurred. No cases occurred in vaccinees who received HAVRIX.

Using additional virological and serological analyses post hoc, the efficacy of HAVRIX was confirmed. Up to 3 additional cases of very mild clinical illness may have occurred in vaccinees. Using available testing, these illnesses could neither be proven nor disproven to have been caused by HAV. By including these as cases, the calculated efficacy rate for prevention of clinical hepatitis A would be 84% (95% confidence intervals 60% to 94%).

In a study designed to interrupt an epidemic of hepatitis A among Native Americans in Alaska, vaccination with a single dose of HAVRIX (1440 EL.U./mL in adults, 720 EL.U./0.5 mL in children and adolescents) appeared to be efficacious.[4]

Immunogenicity in Children and Adolescents: *Immune Response to HAVRIX 720 EL.U./0.5 mL in Children Vaccinated Beginning at 11 Months of Age:* In a prospective, open-label, multicenter study, 1,085 children were enrolled into one of 5 groups:

(1) children 11 to 13 months of age who received HAVRIX on a 0- and 6-month schedule;

(2) children 15 to 18 months of age who received HAVRIX on a 0- and 6-month schedule;

(3) children 15 to 18 months of age who received HAVRIX coadministered with INFANRIX® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) and OMNIHIB™ Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate) [Hib conjugate vaccine (PRP-T)] at month 0 and HAVRIX at month 6;

(4) children 15 to 18 months of age who received INFANRIX coadministered with Hib conjugate vaccine (PRP-T) at month 0 and HAVRIX at months 1 and 7;

(5) children 23 to 25 months of age who received HAVRIX on a 0- and 6-month schedule.

The anti-hepatitis A antibody vaccine responses and geometric mean antibody titers (GMTs), calculated on responders for groups 1, 2, and 5 are presented in Table 1. Vaccine response rates were similar among the three age groups that received HAVRIX. One month after the second dose of HAVRIX, the GMT in each of the younger age groups (11 to 13 and 15 to 18 months of age) was shown to be similar to that achieved in the 23 to 25 months of age group.

Table 1. Anti-hepatitis A Immune Response Following Two Doses of HAVRIX 720 EL.U./0.5 mL Administered 6 Months Apart in Children Given the First Dose of HAVRIX at 11 to 13 Months of Age, 15 to 18 Months of Age, or 23 to 25 Months of Age

Age group	N	Vaccine Response (%)	Vaccine Response 95% CI	GMT (mIU/mL)
11-13 months (Group 1)	218	99	97, 100%	1,461*
15-18 months (Group 2)	200	100	98, 100%	1,635*
23-25 months (Group 5)	211	100	98, 100%	1,911

Vaccine response = Seroconversion in children initially seronegative or at least the maintenance of the pre-vaccination anti-HAV concentration in initially seropositive children.
GMT = Geometric mean antibody titer.
*Calculated on vaccine responders one month post-dose 2. GMTs in children 11 to 13 months of age and 15 to 18 months of age were non-inferior (similar) to the GMT in children 23 to 25 months of age (i.e., the lower limit of the two-sided 95% CI on the GMT ratio for Group 1/Group 5 and for Group 2/Group 5 were both ≥0.5).

Immunogenicity in Children and Adolescents: *Immune Response to HAVRIX 360 EL.U. in Children Vaccinated Beginning at 2 Years of Age:* In 6 clinical studies of subjects 2 to 18 years of age (n = 762) who received 2 doses of HAVRIX (360 EL.U.) given 1 month apart, the GMT ranged from 197 to 660 mIU/mL. Ninety-nine percent of subjects seroconverted following 2 doses. When a booster (third) dose of HAVRIX 360 EL.U. was administered 6 months following the initial dose, all subjects were seropositive 1 month following the booster dose, with GMTs rising to a range of 3,388 to 4,643 mIU/mL. In 1 study in which children were followed for an additional 6 months, all subjects remained seropositive. Solicited adverse effects were similar in frequency and nature to those seen following administration of ENGERIX-B.

Immune Response to HAVRIX 720 EL.U./0.5 mL in Children Vaccinated Beginning at 2 Years of Age: In 4 clinical studies, children and adolescents (n = 314), ranging from 2 to 19 years of age, were immunized with 2 doses of HAVRIX 720 EL.U./0.5 mL given 6 months apart. One month after the first dose, seroconversion ranged from 96.8% to 100%, with GMTs of 194 mIU/mL to 305 mIU/mL. In studies in which sera were obtained 2 weeks following the initial dose, seroconversion ranged from 91.6% to 96.1%. One month following a booster dose at month 6, all subjects were seropositive, with GMTs ranging from 2,495 mIU/mL to 3,644 mIU/mL.[5]

In 1 additional study in which the booster dose was delayed until 1 year following the initial dose, 95.2% of the subjects were seropositive just prior to administration of the booster dose. One month later, all subjects were seropositive, with a GMT of 2,657 mIU/mL.[5]

Also, HAVRIX has been found to be highly efficacious in a clinical study of children at high risk of HAV infection (see Protective Efficacy, above).

Immunogenicity in Adults: In 3 clinical studies involving over 400 healthy adults 18-50 years of age given a single 1440 EL.U. dose of HAVRIX, specific humoral antibodies against HAV were elicited in more than 96% of subjects when measured 1 month after vaccination. By day 15, 80% to 98% of vaccinees had already seroconverted (anti-HAV ≥20 mIU/mL [the lower limit of antibody measurement by current assay]). Geometric mean titers (GMTs) of seroconverters ranged from 264 to 339 mIU/mL at day 15 and increased to a range of 335 to 637 mIU/mL by 1 month following vaccination.[5]

The GMTs obtained following a single dose of HAVRIX are at least several times higher than that expected following receipt of immune globulin (IG).

In a clinical study using 2.5 to 5 times the standard dose of IG (standard dose = 0.02 to 0.06 mL/kg), the GMT in recipients was 146 mIU/mL at 5 days post-administration, 77 mIU/mL at month 1, and 63 mIU/mL at month 2.[5]

In 2 clinical trials in which a booster dose of 1440 EL.U. was given 6 months following the initial dose, 100% of vaccinees (n = 269) were seropositive 1 month after the booster dose, with GMTs ranging from 3,318 mIU/mL to 5,925 mIU/mL. The titers obtained from this additional dose approximate those observed several years after natural infection.

In a subset of vaccinees (n = 89), a single dose of HAVRIX 1440 EL.U. elicited specific anti-HAV neutralizing antibodies in more than 94% of vaccinees when measured 1 month after vaccination. These neutralizing antibodies persisted until month 6. One hundred percent of vaccinees had neutralizing antibodies when measured 1 month after a booster dose given at month 6.

Immunogenicity of HAVRIX was studied in subjects with chronic liver disease of various etiologies. 189 healthy adults and 220 adults with either chronic hepatitis B (n = 46), chronic hepatitis C (n = 104), or moderate chronic liver disease of other etiology (n = 70) were vaccinated with HAVRIX 1440 EL.U. on a 0- and 6-month schedule. The last group consisted of alcoholic cirrhosis (n = 17), autoimmune hepatitis (n = 10), chronic hepatitis/cryptogenic cirrhosis (n = 9), hemochromatosis (n = 2), primary biliary cirrhosis (n = 15), primary sclerosing cholangitis (n = 4), and unspecified (n = 13). At each time point, GMTs were lower for subjects with chronic liver disease than for healthy subjects. At month 7, the GMTs ranged from 478 mIU/mL (chronic hepatitis C) to 1,245 mIU/mL (healthy), as determined by a commercial ELISA. The relevance of these data to the duration of protection afforded by HAVRIX is unknown. One month after the first dose, seroconversion rates in adults with chronic liver disease were lower than in healthy adults. However, 1 month after the booster dose at month 6, seroconversion rates were similar in all groups; rates ranged from 94.7% to 98.1%.

The duration of immunity following a complete schedule of immunization with HAVRIX has not been established.

Immune Response to Concomitantly Administered Vaccines: The concomitant administration of Hib conjugate vaccine (PRP-T) and INFANRIX with HAVRIX was evaluated in children receiving their first dose of HAVRIX at 15 to 18 months of age followed by a second dose of HAVRIX 6 months later. One month after the second dose of HAVRIX, the anti-

hepatitis A vaccine response (100%) in those receiving the first dose of HAVRIX coadministered with INFANRIX and Hib conjugate vaccine (PRP-T) was shown to be non-inferior to that achieved (100%) in 15 to 18 month olds who received HAVRIX alone (lower limit of 95% CI on difference for coadministered vaccine group minus HAVRIX alone group >-5%).

One month after vaccination with Hib conjugate vaccine (PRP-T), the seroprotection rates for Hib were shown to be non-inferior in subjects who received Hib conjugate vaccine (PRP-T) concomitantly with their first dose of HAVRIX (100% achieved ≥1 mcg/mL of anti-PRP antibody; 95% CI, 97 to 100%) as compared to those who did not receive HAVRIX (100% achieved ≥1 mcg/mL of anti-PRP antibody; 95% CI, 97 to 100%). Both groups received INFANRIX concomitantly with Hib conjugate vaccine (PRP-T) ± HAVRIX. Insufficient data are available to assess the immune response of a fourth dose of DTaP vaccine when administered with HAVRIX.

There are limited data on the coadministration of HAVRIX with other vaccines.

INDICATIONS AND USAGE

HAVRIX is indicated for active immunization of persons ≥12 months of age against disease caused by hepatitis A virus (HAV). Primary immunization should be administered at least 2 weeks prior to expected exposure to HAV. The Advisory Committee on Immunization Practices (ACIP) has issued recommendations for hepatitis A vaccination for persons who are at increased risk for infection and for any person wishing to obtain immunity (www.cdc.gov).[6]

When passive protection against hepatitis A is required either following exposure to hepatitis A virus or in persons requiring both immediate and long-term protection, HAVRIX may be administered concomitantly with IG with different syringes and at different injection sites.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including neomycin, is a contraindication (see DESCRIPTION). This vaccine is contraindicated in patients with previous hypersensitivity to any hepatitis A-containing vaccine.

WARNINGS

There have been rare reports of anaphylaxis/anaphylactoid reactions following commercial use of the vaccine.

The tip cap and the rubber plunger of the needleless prefilled syringes contain dry natural latex rubber that may cause allergic reactions in latex sensitive individuals. The vial stopper is latex-free.

Hepatitis A has a relatively long incubation period (15 to 50 days). Hepatitis A vaccine may not prevent hepatitis A infection in individuals who have an unrecognized hepatitis A infection at the time of vaccination. Additionally, it may not prevent infection in individuals who do not achieve protective antibody titers (although the lowest titer needed to confer protection has not been determined).

PRECAUTIONS

General: Prior to immunization with HAVRIX, the patient's current health status and medical history should be reviewed. The physician should review the patient's immunization history for possible vaccine sensitivity, previous vaccination-related adverse reactions and occurrence of any adverse–event-related symptoms and/or signs, in order to determine the existence of any contraindication to immunization with HAVRIX and to allow an assessment of benefits and risks. Appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of the vaccine. Epinephrine injection (1:1,000) and other appropriate agents used for the control of immediate allergic reactions must be immediately available.

A separate, sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent the transmission of other infectious agents from person to person. Needles should be disposed of properly and should not be recapped.

As with any vaccine, if administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the expected immune response may not be obtained.

Information for Vaccine Recipients and Guardians: Vaccine recipients and guardians should be informed by their healthcare provider of the potential benefits and risks of immunization with HAVRIX. When educating vaccine recipients and guardians regarding potential side effects, clinicians should emphasize that HAVRIX contains non-infectious killed viruses and cannot cause hepatitis A infection.

Vaccine recipients and guardians should be instructed to report any severe or unusual adverse reactions to their healthcare provider.

The vaccine recipients or guardian should be given the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the CDC website (www.cdc.gov/nip).

Drug Interactions: HAVRIX may be given concurrently with Hib conjugate vaccines in children 15 to 18 months of age (see CLINICAL PHARMACOLOGY and ADVERSE REACTIONS). The safety of HAVRIX given concomitantly with INFANRIX has been evaluated (see ADVERSE REACTIONS). Insufficient data are available to assess the immune response of a fourth dose of DTaP vaccine when administered with HAVRIX.

There are limited data to assess the concomitant use of HAVRIX with other vaccines. (See Immune Response to Concomitantly Administered Vaccines.)

Carcinogenesis, Mutagenesis, Impairment of Fertility: HAVRIX has not been evaluated for its carcinogenic potential, mutagenic potential, or potential for impairment of fertility.

Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with HAVRIX. It is also not known whether HAVRIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. HAVRIX should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether HAVRIX is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when HAVRIX is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of HAVRIX have been evaluated in 20,436 subjects 1 year to 18 years of age. (See CLINICAL PHARMACOLOGY for immunogenicity and efficacy data. See DOSAGE AND ADMINISTRATION for recommended dosage.)

The safety and effectiveness of HAVRIX have not been established in subjects less than 12 months of age.

Geriatric Use: Clinical studies of HAVRIX did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in overall safety between these subjects and younger adult subjects.

ADVERSE REACTIONS

The safety of HAVRIX has been evaluated in clinical trials involving more than 31,000 individuals receiving doses ranging from 360 EL.U. to 1440 EL.U. and during postmarketing experience in Europe. As with all pharmaceuticals, however, it is possible that expanded commercial use of the vaccine could reveal rare adverse events not observed in clinical studies.

The frequency of solicited adverse events tended to decrease with successive doses of HAVRIX. Most events reported were considered by the subjects as mild and did not last for more than 24 hours.

Of solicited adverse events in clinical trials, the most frequently reported by volunteers was injection-site soreness (56% of adults and 21% of children); however, less than 0.5% of soreness was reported as severe. Headache was reported by 14% of adults and less than 9% of children. Other solicited and unsolicited events occurring during clinical trials are listed below:

Incidence 1% to 10% of Injections:

Local Reactions at Injection Site: Induration, redness, swelling.

Body as a Whole: Fatigue, fever (>37.5°C), malaise.

Gastrointestinal: Anorexia, nausea.

Incidence <1% of Injections:

Local Reaction at Injection Site: Hematoma.

Dermatologic: Pruritus, rash, urticaria.

Respiratory: Pharyngitis, other upper respiratory tract infections.

Gastrointestinal: Abdominal pain, diarrhea, dysgeusia, vomiting.

Musculoskeletal: Arthralgia, elevation of creatine phosphokinase, myalgia.

Hematologic: Lymphadenopathy.

Central Nervous System: Hypertonic episode, insomnia, photophobia, vertigo.

Additional Safety Data: Safety data were obtained from 2 additional sources in which large populations were vaccinated. In an outbreak setting in which 4,930 individuals were immunized with a single dose of either 720 EL.U. or 1440 EL.U. of HAVRIX, the vaccine was well

tolerated and no serious adverse events due to vaccination were reported. Overall, less than 10% of vaccinees reported solicited general adverse events following the vaccine. The most common solicited local adverse event was pain at the injection site, reported in 22.3% of subjects at 24 hours and decreasing to 2.4% by 72 hours. In a field efficacy trial, 19,037 children received the 360 EL.U. dose of HAVRIX. The most commonly reported adverse events following administration of HAVRIX were injection-site pain (9.5%) and tenderness (8.1%), which were reported following first doses of HAVRIX. Other adverse events were infrequent and comparable to the control vaccine ENGERIX-B. Additionally, no serious adverse events due to the vaccine were reported. The large trial further allowed for analysis of rare adverse events, including hospitalization and death. No significant differences were found between the cohorts.

In subjects with chronic liver disease, HAVRIX was safe and well tolerated. Local injection site reactions were similar among all 4 groups, and no serious adverse reactions attributed to the vaccine were reported in subjects with chronic liver disease.

Safety Data for HAVRIX 720 EL.U./0.5 mL Beginning at 11 Months of Age: In the multicenter study described under CLINICAL PHARMACOLOGY, parents/guardians recorded local and general symptoms on diary cards for 4 days (Days 0 to 3) after vaccination. In the 3 groups of children who received HAVRIX alone, safety data were available for 723 children who received 1,396 documented doses of HAVRIX. Additional safety data were available for 181 children who received HAVRIX coadministered with INFANRIX and Hib conjugate vaccine (PRP-T). Most adverse events were mild and transient. The frequencies of solicited local and systemic reactions following receipt of HAVRIX were monitored during the 4-day observation period.

The following rates of solicited adverse events in children who received their first dose of HAVRIX alone at between 11 and 25 months of age were observed. Among local reactions: pain was reported in 15-21% of subjects, redness in 16-21%, swelling in 8% of subjects. Among general reactions, irritability was reported in 24-36% of subjects, loss of appetite in 16-19% of subjects, drowsiness in 15-17% of subjects and fever >39.5°C in ≤2% of subjects. Following the booster dose of HAVRIX, among local reactions: pain was reported in 16-21% of subjects, redness in 17-22%, swelling in 8-10% of subjects. Following the booster dose of HAVRIX, among general reactions, irritability was reported in 19-29% of subjects, loss of appetite in 14-18% of subjects, drowsiness in 13-16% of subjects and fever >39.5°C in ≤1% of subjects.

Drowsiness and loss of appetite occurred at statistically significantly higher rates in subjects 15 to 18 months of age who received Hib conjugate vaccine (PRP-T) and INFANRIX concomitantly with HAVRIX as compared to subjects 15 to 18 months of age who received Hib conjugate vaccine (PRP-T) and INFANRIX (drowsiness 34% and 22% and loss of appetite 29% and 19%, respectively). With the exception of fever (>39.5°C), the solicited general symptoms occurred at statistically significantly higher rates in subjects 15 to 18 months of age who received Hib conjugate vaccine (PRP-T) and INFANRIX concomitantly with HAVRIX as compared to subjects 15 to 18 months of age who received HAVRIX alone (irritability 46% and 30%, drowsiness 34% and 17%, and loss of appetite 29% and 17%, respectively).

A febrile seizure was reported in an 18-month old subject two days after receiving the first dose of HAVRIX. Other serious adverse events reported during the course of this study included a single case each of hepatitis ~5 months post dose 1, insulin-dependent diabetes ~4 months post dose 1, and Kawasaki's disease ~3½ months post dose 1. The association of these events with vaccination is unknown.

Postmarketing Reports: Rare voluntary reports of adverse events in people receiving HAVRIX that have been reported since market introduction of the vaccine include the following:

Local: Localized edema.

While no causal relationship has been established, the following rare events have been reported:

Body as a Whole: Anaphylaxis/anaphylactoid reactions, somnolence.

Cardiovascular: Syncope.

Hepatobiliary: Jaundice, hepatitis.

Dermatologic: Erythema multiforme, hyperhydrosis, angioedema.

Respiratory: Dyspnea.

Hematologic: Lymphadenopathy, thrombocytopenia.

Central Nervous System: Convulsions, encephalopathy, dizziness, neuropathy, myelitis, paresthesia, Guillain-Barré syndrome, multiple sclerosis.

Other: Congenital abnormality.

Reporting of Adverse Events: The US Department of Health and Human Services has established the Vaccine Adverse Events Reporting System (VAERS) to accept reports of suspected adverse events after the administration of any vaccine, including, but not limited to, the reporting of events required by the National Childhood Vaccine Injury Act of 1986. The toll-free number for VAERS forms and information is 1-800-822-7967.[7] Reporting forms may also be obtained at the VAERS website at www.vaers.hhs.gov.

DOSAGE AND ADMINISTRATION

HAVRIX should be administered by intramuscular injection. *Do not inject intravenously, intradermally, or subcutaneously.* In adults, the injection should be given in the deltoid region. HAVRIX should not be administered in the gluteal region; such injections may result in suboptimal response.

Children and Adolescents: Primary immunization for children and adolescents (12 months through 18 years of age) consists of a single dose of 720 EL.U. in 0.5 mL and a booster dose (720 EL.U. in 0.5 mL) should be administered anytime between 6 and 12 months later.

Adults: Primary immunization for adults consists of a single dose of 1440 EL.U. in 1 mL and a booster dose (1440 EL.U. in 1 mL) should be administered anytime between 6 and 12 months later.

For all age groups, a booster dose should be administered anytime between 6 and 12 months after the initiation of the primary dose in order to ensure the highest antibody titers.

HAVRIX may be administered concomitantly with IG, although the ultimate antibody titer obtained is likely to be lower than when the vaccine is given alone.

For individuals with clotting factor disorders at risk of hematoma formation following intramuscular injection, the ACIP recommends that when any intramuscular vaccine is indicated for such patients, ". . . the vaccine should be administered intramuscularly if, in the opinion of a physician familiar with the patient's bleeding risk, the vaccine can be administered with reasonable safety by this route. If the patient receives antihemophilia or other similar therapy, intramuscular vaccinations can be scheduled shortly after such therapy is administered. A fine needle (≤23 gauge) should be used for the vaccination and firm pressure applied to the site, without rubbing, for ≥2 minutes. The patient or family should be instructed concerning the risk for hematoma from the injection."[8]

When concomitant administration of other vaccines or IG is required, they should be given with different syringes and at different injection sites.

In those with an impaired immune system, adequate anti-HAV response may not be obtained after the primary immunization course. Such patients may therefore require administration of additional doses of vaccine.

Preparation for Administration: Shake vial or syringe well before withdrawal and use. Parenteral drug products should be inspected visually for particulate matter or discoloration prior to administration. With thorough agitation, HAVRIX is a slightly turbid white suspension. Discard if it appears otherwise.

The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used. After removal of the appropriate volume from a single-dose vial, any vaccine remaining in the vial should be discarded.

STORAGE

Store refrigerated between 2° and 8°C (36° and 46°F). Do not freeze; discard if product has been frozen. Do not dilute to administer.

HOW SUPPLIED

HAVRIX is supplied as a slightly turbid white suspension in vials and prefilled TIP-LOK® syringes.

720 EL.U./0.5 mL in Single-Dose Vials and Prefilled Syringes (Preservative Free Formulation)

NDC 58160-825-11 Package of 10 Single-Dose Vials

NDC 58160-825-46 Package of 5 Prefilled Disposable TIP-LOK Syringes (packaged without needles)

1440 EL.U./mL in Single-Dose Vials and Prefilled Syringes (Preservative Free Formulation)

NDC 58160-826-11 Package of 10 Single-Dose Vials

NDC 58160-826-46 Package of 5 Prefilled Disposable TIP-LOK Syringes (packaged without needles)

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Manufactured by **GlaxoSmithKline Biologicals,** Rixensart, Belgium, US License No. 1617
Distributed by **GlaxoSmithKline,** Research Triangle Park, NC 27709

December 2006 HA:L21