(/drug-shortages/280)Hepatitis A Vaccine Inactivated

AHFS Class: 80:12 — Vaccines (tofc-80)

Hepatitis A Vaccine Inactivated *(AHFS DI)*

Hepatitis A Vaccine Inactivated **Hepatitis A and Hepatitis B (Recombinant) Vaccine**

Alert:

On January 5, 2026, the US Department of Health and Human Services (HHS) announced the approval of a revised US childhood and adolescent immunization schedule (https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html (https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html)). Under the revised recommendations, CDC continues to organize the childhood immunization schedule in three distinct categories (Immunizations Recommended for All Children, Immunizations Recommended for Certain High-Risk Groups or Populations, and Immunizations Based on Shared Clinical Decision-Making) but changes individual vaccine placement within those categories. For additional information, see https://www.hhs.gov/press-room/cdc-acts-presidential-memorandum-update-childhood-immunization-schedule.html (https://www.hhs.gov/press-room/cdc-acts-presidential-memorandum-update-childhood-immunization-schedule.html) .

Introduction

Hepatitis A vaccine is an inactivated vaccine containing cell culture-adapted, inactivated hepatitis A virus (HAV).[1,171,]

Uses

▪ Prevention of Hepatitis A Infection

Hepatitis A vaccine inactivated (hepatitis A vaccine) is used to stimulate active immunity to hepatitis A virus (HAV) infection in individuals 12 months of age and older.[1,171,] Hepatitis A virus vaccine is commercially available in the US as monovalent (i.e., single-antigen) vaccines (Havrix®, Vaqta®)[1,171,] and in a fixed-combination with hepatitis B vaccine (HepA-HepB; Twinrix®).[186,] The fixed combination HepA-HepB vaccine is only indicated for use in adults (18 years of age or older).[186,]

Hepatitis A is a viral infection caused by HAV; it is one of several types of viral hepatitis infections.[211,212,] Transmission of HAV occurs via the fecal-oral route, usually through close person-to-person contact or consumption of contaminated food or water.[210,211,213,] Levels of endemic HAV transmission are low in the United States, primarily due to successful vaccination efforts after the introduction of the hepatitis A vaccine in 1996.[212,213,] However, large-scale outbreaks have been reported due to common-source food exposures and person-to-person spread among at-risk populations (e.g., drug users, people experiencing homelessness, men who have sex with men).[210,212,213,] Low adult hepatitis A vaccination coverage and high population susceptibility allow continued outbreaks to occur.[210,] International travelers are also at increased risk for HAV infection, particularly if they are traveling to rural areas in regions with higher levels of endemic transmission (e.g., Central and South America, Africa, Asia).[211,212,213,] Additional at-risk populations include people who anticipate close personal contact with an international adoptee, people whose jobs increase the risk of exposure (i.e., those who work with HAV-infected non-human primates or material containing HAV in a research setting), and people in settings where services to adults are provided (e.g., group homes for people with developmental disabilities, syringe service programs, correctional facilities during outbreaks).[210,211,212,]

In patients <6 years of age, most HAV infections are asymptomatic; however, the majority of older children and adults will present with abrupt onset of fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice.[212,] In healthy persons, HAV infection usually causes mild, self-limiting illness, but patients >40 years of age, immunocompromised patients, and patients with chronic liver disease or other underlying health conditions may be at increased risk for serious complications of HAV infection, including liver failure and death.[210,211,]

Clinical Experience

Primary Immunization in Children and Adolescents.

Efficacy of Havrix® in the pediatric population has been established in a double-blind, randomized controlled study in children 1 to 16 years of age in Thailand who were at high risk of HAV infection.[1,] A total of 19,037 children received Havrix® (360 EL.U) and 19,120 children received a control vaccine (hepatitis B vaccine [recombinant] 10 mcg); both vaccines were administered in 2 doses at 0 and 1 month.[1,] Based on surveillance data for up to 8 months following vaccination, the calculated vaccine efficacy rate for Havrix® was 94%.[1,] In the group receiving Havrix®, 2 cases of clinical hepatitis A occurred compared with 32 cases in the control group.[1,] Results of an additional pos-hoc analysis which included 3 possible cases of mild clinical hepatitis A demonstrated a calculated vaccine efficacy rate of 84%.[1,]

Immunogenicity of Havrix® in children and adolescents was evaluated in a prospective, open-label, multicenter study in 1084 children 11–25 months of age who received a two-dose series of Havrix® (two doses of 720 EL.U./0.5 mL given 6 months apart; first dose at 11–13 months, 15–18 months, or 23–25 months).[1,] Vaccine response rates of 99–100% were observed in this patient population.[1,] Four additional clinical studies examined vaccine response rates in a total of 314 children and adolescents 2–19 years of age immunized with 2 doses of Havrix® 720 EL.U./0.5 mL given 6 months apart.[1,] One month after the initial dose of Havrix®, seroconversion rates ranged from 96.8–100%; one month following the second dose at month 6, all patients were seropositive for anti-HAV antibodies.[1,] In an additional study in which the second dose of Havrix® was delayed until 1 year following the initial dose, 95.2% of patients were seropositive just prior to administration of the second dose, and all patients were seropositive 1 month after the second dose.[1,]

Immunogenicity and efficacy of Vaqta® were evaluated in a randomized, double-blind, placebo-controlled study enrolling 1037 healthy children and adolescents 2–16 years of age in a US community with recurrent outbreaks of hepatitis A (the Monroe Efficacy Study).[40,171] Patients were randomized to receive a single 25 U dose of Vaqta® or placebo.[171] Within 4 weeks of vaccination with Vaqta®, over 99% of patients who were initially seronegative achieved seroconversion.[171] The onset of seroconversion was shown to parallel the onset of protection against clinical hepatitis A disease.[171] Protective efficacy of the vaccine was observed to be 100%; 21 cases of clinically confirmed hepatitis A were reported in the placebo group ≥50 days after vaccination, whereas 0 cases were reported in the group that received active vaccine.[171] Following demonstration of protection with a single dose of the vaccine, an additional dose was administered to a subset of patients 6, 12, or 18 months after reception of the primary dose.[171] Seroconversion rates just prior to the second vaccine dose at 6, 12, or 18 months were 97, 91, or 90%, respectively.[171] Seroconversion rates were 100% 4 weeks after the second vaccine dose, irrespective of the interval between the first and second dose.[171] Detectable levels of anti-HAV antibodies were present for at least 10 years post-vaccination in all children who received 2 doses of Vaqta®.[171] No cases of clinically confirmed hepatitis A disease ≥50 days after vaccination were reported when vaccine recipients from the Monroe Efficacy Study were followed for up to 9 years.[171,216]

Efficacy of Vaqta® in other pediatric age groups was established based on immunogenicity measured 4–6 weeks after vaccination.[171] In one clinical trial of children 12–23 months of age who received Vaqta® with or without other childhood vaccines, seroconversion rates were 96% after a first dose of Vaqta® and 100% after a second dose.[171] In another trial of healthy children 12–15 months of age who received Vaqta® with or without other vaccines, seropositivity rates for anti-HAV antibodies following the second dose of Vaqta® ranged from 99.4–100%.[171] An additional study in children 15 months of age who received Vaqta® with or without other vaccines found seropositivity rates of 100% 4 weeks after the second vaccine dose.[171] Combined immunogenicity data from 11 clinical studies (including the Monroe Efficacy Study) in patients 2–18 years of age found overall seroconversion rates of 97% following a first dose of Vaqta® and 100% following a second dose of Vaqta® administered 6 months after the first dose.[171]

Primary Immunization in Adults.

Over 400 healthy adults 18–50 years of age received a single dose of Havrix® 1440 EL.U. in 3 clinical studies; specific humoral antibodies against HAV were elicited in more than 96% of patients at 1 month post-vaccination.[1] The majority of patients (80–98%) seroconverted by day 15 post-vaccination.[1] In 2 clinical trials enrolling 269 patients, a second dose of Havrix® 1440 EL.U. was administered 6 months following the initial dose; all patients in these studies were found to be seropositive 1 month following the second vaccine dose.[1] One study comparing seroconversion rates among healthy patients and patients with chronic liver disease (hepatitis B, hepatitis C, or other moderate chronic liver disease) found that seroconversion rates were similar between groups 1 month after completion of a 2-dose series of Havrix® 1440 EL.U. (94.7–98.1%).[1] A long-term follow-up study of patients who received a 2-dose series of Havrix® 1440 EL.U. (with doses given 6–12 months apart) found that >97% of patients maintained detectable anti-HAV antibody levels up to 20 years post-vaccination.[217]

Efficacy of Vaqta® in adults ≥19 years of age was established based on pooled immunogenicity data from 5 randomized clinical studies.[171] In these studies, administration of Vaqta® 50 U resulted in seroconversion rates of 95% at 4 weeks after the first vaccine dose and 99.9% at 4 weeks following a second vaccine dose given 6 months after the first.[171] At 2 weeks following the first dose of Vaqta® 50 U, seroconversion rates of 69.2% were observed.[171] When second vaccine doses were given 12 or 18 months following the first dose, seroconversion rates 4 weeks after the second dose were 98 and 100%, respectively.[171] Most patients (99.4%) who received a 2-dose series of Vaqta® with doses given 6 months apart maintained detectable levels of anti-HAV antibodies at 6 years.[171]

A randomized, double-blind study in 537 healthy adults 18–83 years of age evaluated the immune response to a booster dose of Havrix® or Vaqta® given at 6 or 12 months following an initial dose of Havrix®.[171] After their initial dose of Havrix®, 232 patients received a dose of Vaqta® at 6 months, 124 patients received a dose of Vaqta® at 12 months, 118 patients received a second dose of Havrix® at 6 months, and 63 patients received a second dose of Havrix® at 12 months.[171] A booster response (defined as a ≥10-fold rise in titers following booster administration and a post-booster titer ≥100 mIU/mL) at 4 weeks following the second vaccine dose was observed in 86.1% of patients who received Vaqta® for their second dose and 80.1% of patients who received Havrix® for their second dose; seropositivity rates were >99% regardless of the product used for the second dose.[171]

Postexposure Prophylaxis.

Efficacy of hepatitis A vaccine for **postexposure prophylaxis [off-label]**† of HAV has been evaluated in a randomized, double-blind, noninferiority trial in susceptible individuals 2–40 years of age who were household or child-care center contacts of index patients with HAV.[199] Individuals were randomized to receive a single dose of monovalent hepatitis A vaccine (age-appropriate dose of Vaqta®) or IM immune globulin (0.02 mL/kg) within 14 days after exposure to a laboratory-confirmed index case of HAV.[199] The primary end point was laboratory-confirmed symptomatic HAV occurring between 15–56 days after exposure.[199] In the per-protocol analyses, HAV was confirmed in 4.4% of those who received the vaccine and 3.3% of those who received IM immune globulin.[199] The relative risk of HAV among vaccine recipients was noninferior to that reported for IM immune globulin recipients.[199]

In a study in Naples, Italy, hepatitis A vaccine (Havrix®) was administered to family contacts of individuals with primary HAV infection (index cases) for **postexposure prophylaxis [off-label]**†.[185] The vaccine was administered to family contacts who were 1–40 years of age (1440-unit dose in adolescents and adults and 720-unit dose in children 1–11 years of age) and was given within 8 days of symptom onset in the index cases.[185] During 45 days of follow-up, secondary cases of HAV infection occurred in 13.3% of households in the unvaccinated group and 2.8% of households in the vaccinated group; the protective efficacy of the vaccine was 79%.[185]

Clinical Perspective

Primary Vaccination.

The American Academy of Pediatrics (AAP) and other organizations recommend primary vaccination with a 2-dose series of hepatitis A vaccine in children 12 through 23 months, unless contraindicated.[210,214,218,304] Hepatitis A vaccination is not routinely performed in patients <12 months of age, as this could result in a suboptimal immune response (particularly in infants with passively acquired maternal antibodies).[213,214] The Centers for Disease Control and Prevention (CDC) recommend the hepatitis A vaccine for children at high risk of serious illness or after shared clinical decision-making with a healthcare provider.[214] Children and adolescents 2–18 years of age who have not previously received the hepatitis A vaccine (i.e., those requiring catch-up vaccination) should be vaccinated against HAV if there are no contraindications.[210,214,218,304] Doses of hepatitis A vaccine should be administered a minimum of 6 months apart.[214,304]

The CDC and Advisory Committee on Immunization Practices (ACIP) state that any person ≥19 years of age who is not fully vaccinated against HAV and requests vaccination should be vaccinated with either a 2-dose series of hepatitis A vaccine or a 3-dose series of HepA-HepB vaccine (if vaccination against both hepatitis A and hepatitis B is desired).[210,215,] Vaccination against HAV is specifically recommended in adults who are not fully vaccinated against HAV who have specific risk factors for HAV infection or severe HAV disease.[215,] These at-risk adult populations include: people with chronic liver disease (including hepatitis B, hepatitis C, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, or ALT or AST >2 times the upper limit of normal); people with HIV infection; men who have sex with men; users of injection or non-injection drugs; people experiencing homelessness; people with occupational exposure risks (i.e., people who work with HAV-infected nonhuman primates or laboratory materials containing HAV); people who plan to travel to countries with high or intermediate HAV endemicity; people who will have close, personal contact with an international adoptee within the first 60 days of arrival from a country with high or intermediate HAV endemicity; pregnant people (if at risk for infection or severe outcome from infection); and people in settings where a high proportion of people have risk factors for HAV infection (e.g., healthcare settings that serve drug users, homeless shelters, group homes or nonresidential day care facilities for developmentally disabled people).[210,215,] Adults ≥18 years of age may receive the HepA-HepB combination vaccine as a 3-dose or 4-dose series if primary vaccination against both hepatitis A and hepatitis B is desired.[214,304,]

Hepatitis A vaccination is recommended for all HIV-infected patients ≥1 year of age.[202,219,220,] The ACIP states that hepatitis A vaccination should not be delayed in patients with low CD4 cell counts; however, HIV-specific guidelines from the National Institutes of Health (NIH), the HIV Medicine Association, and the Infectious Diseases Society of America state that, for adults with CD4 count <200 cells/mm^3 who do not have ongoing risk for HAV, waiting for a CD4 count >200 cells/mm^3 prior to vaccination is an option.[210,219,] Because the response to the vaccine may be reduced in people with HIV who are immunosuppressed, postvaccination serologic testing is recommended for all HIV-infected patients ≥1 month after completing the hepatitis A vaccination series.[210,219,220,] Revaccination of patients with HIV should be considered if an adequate immune response (i.e., ≥10 mIU/mL) was not demonstrated after the initial hepatitis A vaccine series, particularly if the patient's immune status has improved.[210,] The multi-society HIV-specific guideline specifically recommends a third dose of hepatitis A vaccine in adults with CD4 count ≥200 cells/mm^3 who do not demonstrate an adequate antibody response after the primary vaccine series; adults with CD4 count <200 cells/mm^3 who do not demonstrate an adequate antibody response to the primary vaccine series should be revaccinated when their CD4 count increases to >200 cells/mm^3.[219,]

People who work with HAV-infected nonhuman primates and people who work with clinical or nonclinical material containing HAV in a research laboratory setting should be vaccinated against HAV.[210,] Other occupational groups (e.g., healthcare providers, food service handlers) have not been demonstrated to be at increased risk for HAV infection because of occupational exposure; therefore, HAV vaccination on the basis of occupational risk alone is not recommended for these groups.[210,221,]

The CDC and ACIP state that all susceptible people (i.e., those who are unvaccinated or never infected) traveling to countries with high or intermediate HAV endemicity should be vaccinated against HAV or receive immune globulin prior to departure, regardless of the purpose, frequency, or duration of travel.[210,213,] Because the geographic determination of hepatitis A risk is complex and there is potential for foodborne hepatitis A even in low-endemicity countries, some experts advise hepatitis A vaccination for all people traveling outside the US, regardless of destination.[213,] If an unvaccinated patient ≥12 months of age is considering travel to a country with high or intermediate HAV endemicity, the first dose of a hepatitis A vaccine series should be administered as soon as travel is contemplated.[210,214,304,] The rest of the series should then be completed according to the routine vaccination schedule.[210,] The CDC, ACIP, and AAP also recommend administering a single dose of the hepatitis A vaccine to **infants 6–11 months of age [off-label]**† before travel to countries with high or intermediate HAV endemicity.[210,214,218,304,] Patients who receive a dose of the vaccine at 6–11 months of age should be revaccinated with 2 doses of the vaccine (separated by at least 6 months) between 12–23 months of age.[214,218,304,] Vaccination is not recommended for patients <6 months of age; in such patients, IM immunoglobulin is recommended if pretravel prophylaxis is needed.[210,] Unvaccinated adult travelers should receive a single dose of hepatitis A vaccine as soon as travel is considered; if travel is planned in <2 weeks, certain at-risk patients (e.g., people >40 years of age, immunocompromised people, people with chronic liver disease) may also receive a dose of immune globulin at a separate injection site based on provider risk assessment.[210,213,] The hepatitis A vaccine series should be completed according to the routine immunization schedule.[213,] For unvaccinated adult travelers requiring hepatitis A and hepatitis B vaccinations, an accelerated HepA-HepB vaccination schedule may be used (consult guidelines for more details).[213,215,]

The ACIP makes additional recommendations regarding vaccination of internationally adopted children and other immigrants.[303,] In patients vaccinated outside the US who have no (or questionable) vaccination records, ACIP recommends age-appropriate revaccination with the hepatitis A vaccine or serologic testing for IgG antibodies to hepatitis A.[303,] Of note, documentation of certain non-US hepatitis A vaccines (Aimmugen, Twinrix Jr.) should not be accepted as valid documentation of HAV immunity.[303,] Unvaccinated adults anticipating close, personal contact with an international adoptee should receive a first dose of hepatitis A vaccine as soon as the adoption is planned (preferably at least 2 weeks prior to the adoptee's arrival).[210,215,]

The primary hepatitis A vaccination series consists of 2 doses administered at least 6 months apart.[210,] ACIP states that, although it is preferred to complete the vaccination series with doses of the same vaccine (i.e., from the same manufacturer), the series can be completed with vaccine doses from any available manufacturer without a need to repeat doses.[210,] No differences in immunogenicity have been noted when a valid dose of hepatitis A vaccine produced by one manufacturer is followed by a dose of hepatitis A vaccine from another manufacturer when the doses are administered according to the recommended schedule.[210,] The hepatitis A component of Twinrix® is equivalent to a pediatric dose of hepatitis A single-antigen vaccine.[210,] Single-antigen hepatitis A and hepatitis B vaccines may be used in conjunction with the combination vaccine (Twinrix®) to form a complete series of these vaccines; consult the ACIP guidelines for more details on mixed regimens utilizing the combination vaccine.[210,]

Outbreak Control.

During a hepatitis A outbreak, ACIP recommends 1 dose of hepatitis A vaccine for all unvaccinated people ≥1 year of age who are at risk for HAV infection (e.g., drug users, people experiencing homelessness, men who have sex with men) or at risk for severe disease from HAV (e.g., people with chronic liver disease, people with HIV).[210,] A single dose of hepatitis A vaccine is adequate for outbreak control, but the vaccine series should be completed when feasible.[210,] In the event of a community outbreak due to person-to-person transmission, public health officials should consider recommending preexposure hepatitis A vaccination in close congregate settings that provide services for people at risk for HAV (e.g., people incarcerated in correctional facilities, health care settings that serve drug users, homeless shelters, syringe services programs).[210,]

Postexposure Prophylaxis.

The ACIP states that unvaccinated individuals with recent (within 2 weeks) exposure to HAV should receive postexposure prophylaxis with a single dose of hepatitis A vaccine and/or a dose of IM immune globulin as soon as possible.[210,] Consult the ACIP guidelines for additional information on assessing exposure risk and administration of postexposure prophylaxis in specific settings (i.e., child care centers, common-source food exposures and food handlers, settings that provide services to children and adults, healthcare institutions).[210,] Choice of postexposure prophylaxis regimen should be based on patient age and comorbid conditions (e.g., immunocompromised status, chronic liver disease).[210,]

When HAV postexposure prophylaxis is indicated in healthy individuals 12 months to 40 years of age, the ACIP and AAP state that an age-appropriate dose of monovalent hepatitis A vaccine should be used.[210,304,] In healthy adults >40 years of age, the ACIP recommends a dose of hepatitis A vaccine for postexposure prophylaxis; a dose of IM immune globulin may also be administered at the same time as the vaccine, depending on the provider's risk assessment.[210,] For postexposure prophylaxis in patients ≥12 months of age who are immunocompromised or who have chronic liver disease, ACIP and AAP recommend administration of both IM immune globulin and a dose of hepatitis A vaccine.[210,304,] For postexposure prophylaxis in children <12 months of age or patients of any age for whom the vaccine is contraindicated, IM immune globulin alone is recommended.[210,304,]

Although a second dose of hepatitis A vaccine is not required for postexposure prophylaxis, ACIP and AAP recommend completing the vaccination series with a second dose (at least 6 months after the first dose) for long-term immunity.[210,304,] The HepA-HepB combination vaccine is not recommended for use as postexposure prophylaxis.[210,]

Dosage and Administration

▪ General

Dispensing and Administration Precautions

Appropriate medical treatment and supervision must be available to manage potential anaphylactic reactions following vaccination.[1,171,186,]

Ensure procedures are in place to avoid a fall injury from syncope following vaccination.[1,186,]

▪ Administration

Hepatitis A vaccine inactivated (hepatitis A vaccine) is commercially available in the US as monovalent (single-antigen) vaccines (Havrix®, Vaqta®)[1,171,] and in a fixed-combination with hepatitis B vaccine (HepA-HepB; Twinrix®).[186,]

Hepatitis A vaccines are administered by IM injection; do not administer IV, intradermally, or subcutaneously.[1,186,]

To ensure delivery of vaccine into the muscle, IM injections should be made at a 90° angle to the skin using a needle size that is appropriate for the individual's age and body mass, thickness of adipose tissue and muscle at the injection site, and injection technique.[308,]

Since syncope may occur following vaccination, vaccinees should be observed for approximately 15 minutes after the vaccine dose is administered.[303,] If syncope occurs, the patient should be observed until symptoms resolve.[303,] Syncope after vaccination occurs most frequently in adolescents and young adults.[303,]

Do not mix with any other vaccine or product in the same syringe or vial.[1,171,186,]

Hepatitis A vaccine may be given simultaneously with other age-appropriate vaccines during the same health-care visit (using different injection sites).[210,] Hepatitis A vaccine may also be given simultaneously with IM immune globulin, using different injection sites, when indicated.[210,] Injection sites should be separated by ≥1 inch if possible.[307,]

Improper storage or handling of vaccines may result in loss of vaccine potency and reduced immune response in vaccinees.[303,] All vaccines should be inspected upon delivery and monitored during storage to ensure that the appropriate temperature is maintained.[303,] Single antigen hepatitis A vaccine (Havrix®, Vaqta®) or fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) that has been mishandled or has not been stored at the recommended temperature should not be administered.[303,] If there are concerns about mishandling, the manufacturer or state or local health departments should be contacted for guidance on whether the vaccine is usable.[303,]

Havrix®

Havrix® is available in 2 formulations: 0.5 mL single-dose prefilled syringes (containing 720 enzyme-linked immunosorbent assay [ELISA] units per 0.5 mL) for use in individuals 12 months through 18 years of age, and 1 mL single-dose prefilled syringes (containing 1440 ELISA units per mL) in individuals ≥19 years of age.[1,210,]

Do not dilute prior to administration.[1,]

The manufacturer states that the preferred sites for IM injection are the anterolateral aspect of the thigh in young children and the deltoid muscle of the upper arm in older children.[1,] The vaccine should be administered in the deltoid region in adults (≥19 years of age).[1,]

The vaccine should not be injected into the gluteal region since suboptimal response may occur.[1,]

Store Havrix® in the refrigerator between 2–8°C; do not freeze.[1,] Discard if the vaccine has been frozen.[1,]

Before use, the syringe should be shaken well to obtain a homogenous, turbid, white suspension; discard the vaccine if a homogenous suspension does not result.[1,] Do not administer if particulate matter or discoloration is observed.[1,]

Havrix® does not contain any preservatives.[1,]

Vaqta®

Vaqta® is available in 2 formulations: 0.5 mL single-dose vials and prefilled syringes (containing 25 units of hepatitis A virus [HAV] antigen per 0.5 mL) for use in persons aged 12 months through 18 years of age, and 1 mL single-dose vials and prefilled syringes (containing 50 units of HAV antigen per mL) for use in persons ≥19 years of age.[171,]

The manufacturer states that the preferred sites for IM injection are the anterolateral aspect of the thigh for children 12—23 months of age, and the deltoid muscle for adults, adolescents, and children >2 years of age.[171,]

Store Vaqta® in the refrigerator between 2–8°C; do not freeze.[171,]

Before use, the vial or prefilled syringe should be shaken well to obtain a slightly opaque, white suspension; the vaccine should be discarded if a homogenous suspension does not result.[171,] Do not administer if particulate matter or discoloration is observed.[171,]

Vaqta® does not contain any preservatives.[171,]

Twinrix®

Twinrix® is available as 1 mL prefilled syringes for use in adults ≥18 years of age.[186,]

The manufacturer states the vaccine should be administered in the deltoid region.[186,] The vaccine should not be injected into the gluteal region since suboptimal response may occur.[186,]

Store Twinrix® in the refrigerator between 2–8°C.[186,] Do not freeze; discard if the vaccine has been frozen.[186,]

The vaccine should be resuspended before use; the vaccine will have a uniform hazy white appearance when resuspended.[186,] If fine white deposit with a clear colorless layer above is present upon storage, resuspend the product by holding the syringe upright in a closed hand, then vigorously tipping the syringe upside down and back upright again for ≥15 seconds.[186,] If a uniform hazy white suspension is observed, the vaccine is ready to use.[186,] If a uniform hazy white suspension is not observed, repeat tipping for at least another 15 seconds, then inspect the vaccine again.[186,] Do not administer the vaccine if particulate matter or discoloration is observed.[186,]

Twinrix® does not contain any preservatives.[186,]

▪ Dosage

The recommended dose and dosing schedule for hepatitis A vaccine vary according to the individual's age and specific vaccine administered (Havrix® or Vaqta® monovalent vaccines or Twinrix® fixed-combination vaccine).[1,171,186,] Dosage recommendations for the specific preparation used should be followed.[1,171,186,210,]

According to the US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP), the monovalent vaccine chosen for the initial dose should be used for subsequent doses in the same individual whenever possible.[210,] If this is not possible or if the manufacturer of previously administered doses is unknown, then the vaccine that is available should be administered.[210,] This dose is considered valid; it does not need to be repeated.[210,] No differences in immunogenicity have been observed when one dose of hepatitis A vaccine produced by one manufacturer is followed by a dose from a different manufacturer, administered according to the recommended schedule.[210,]

When vaccination against both HAV and hepatitis B virus (HBV) infection is indicated in adults 18 years of age or older, the commercially available fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) can be used.[186,210,]

Consult the CDC/ACIP guidance and immunization schedules for additional information including specific detailed recommendations for catch-up scenarios and management of patients with high-risk conditions.[210,214,215,]

Adults

Primary Immunization Against Hepatitis A Virus (HAV) Infection.

ACIP recommends that any person who has not previously completed the hepatitis A vaccine series may receive the vaccine.[210,] Identification of a risk factor for HAV infection or complication is not necessary for vaccination.[210,]

If Havrix® is used for primary immunization in adults, an initial dose of the age-appropriate preparation should be given followed by a second (booster) dose 6–12 months after the initial dose.[1,210,] Adults ≥19 years of age should receive 1440-unit doses; each dose is 1 mL.[1,]

If Vaqta® is used for primary immunization in adults, an initial dose of the age-appropriate preparation should be given followed by a second (booster) dose 6–18 months after the initial dose.[171,210,] Adults ≥19 years of age should receive 50-unit doses; each dose is 1 mL.[171,] If Havrix® was used for the primary dose, the manufacturer states that a booster dose of Vaqta® may be given at 6–12 months following the primary dose.[171,]

If the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) is used for primary immunization in adults ≥18 years of age or older, three 1-mL doses, administered at 0, 1, and 6 months, should be given.[186,215,] ACIP recommends that the minimum interval should be 4 weeks between dose 1 and dose 2, and 5 months between dose 2 and dose 3.[215,] Each 1-mL dose of the fixed-combination vaccine contains 720 units of hepatitis A viral antigen and 20 mcg of HBsAg.[186,]

Preexposure Vaccination Against HAV Infection in High-risk Groups.

ACIP recommends hepatitis A vaccination in individuals who are not fully vaccinated and who are at risk for HAV infection (e.g., international travelers, men who have sex with men, individuals who use injection or non-injection drugs [i.e., illegal drug users], those with occupational exposure risks, individuals expecting close contact with an international adoptee, those experiencing homelessness) or who are at increased risk of severe disease from HAV infection (e.g., individuals with chronic liver disease or human immunodeficiency virus).[210,] ACIP also recommends hepatitis A vaccination in pregnant women at risk for HAV infection or severe outcome from HAV infection.[210,]

For individuals expecting close personal contact with an international adoptee (e.g., household or regular babysitting) in the first 60 days after arrival of the adoptee from a country with high or intermediate endemic HAV, ACIP recommends that the first dose of hepatitis A vaccine be administered as soon as adoption is planned, preferably ≥2 weeks before the adoptee's arrival.[215,]

For healthy individuals ≤40 years of age who are planning on traveling to an area with high or intermediate HAV endemicity and who have not received the hepatitis A vaccine, ACIP recommends that 1 dose of the vaccine be administered as soon as travel is considered; the vaccine series should be completed according to routine schedule.[210,]

For individuals >40 years of age, individuals with immunocompromising conditions, or those with chronic liver disease who are planning on traveling to an area with high or intermediate HAV endemicity, ACIP recommends that 1 dose of the vaccine be administered as soon as travel is considered.[210,] Individuals traveling in <2 weeks should receive the initial dose of the vaccine and may be administered immune globulin concurrently at a different injection site.[210,] The hepatitis A vaccine series should be completed according to routine schedule.[210,] Consult ACIP for dosage recommendations for immune globulin.[210,]

The recommended hepatitis A vaccine regimens for preexposure prophylaxis are the same as the age-specific regimens recommended for primary immunization.[210,] The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171,]

If the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) is used for hepatitis A vaccination in adults ≥18 years of age or older, three 1-mL doses, administered at 0, 1, and 6 months, should be given.[186,215,] ACIP recommends that the minimum interval should be 4 weeks between dose 1 and dose 2, and 5 months between dose 2 and dose 3.[215,] Alternatively, an accelerated dosing schedule of Twinrix® may be administered for individuals traveling to countries with high or intermediate endemic HAV, with three 1-mL doses, administered at 0, 7, and 21–30 days, followed by a booster dose at 12 months.[215,] Each 1-mL dose of the fixed-combination vaccine contains 720 units of hepatitis A viral antigen and 20 mcg of HBsAg.[186,]

Outbreak Control.

In the setting of an HAV outbreak, ACIP recommends a single dose of the monovalent hepatitis A vaccine (Havrix®, Vaqta®) for all unvaccinated adults who are at risk for HAV infection or at risk for severe disease from HAV.[210,] A single dose of preexposure hepatitis A vaccine has been shown to successfully control HAV outbreaks.[210,]

The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171,]

Postexposure Prophylaxis of HAV Infection.

For **postexposure prophylaxis [off-label]**† in healthy adults (≤40 years of age) exposed to HAV within the past 2 weeks and who have not completed the hepatitis A vaccination series, a single dose of monovalent hepatitis A vaccine (Havrix®, Vaqta®) should be administered as soon as possible.[210,] In adults >40 years of age, immune globulin may be administered in addition to hepatitis A vaccine (at different injection sites) depending on the provider's risk assessment.[210,] When the dose of hepatitis A vaccine administered for postexposure prophylaxis is the first dose the exposed individual has received, a second dose should be administered 6 months after the first dose for long-term immunity; however, the second dose is not required for postexposure prophylaxis.[210,]

For **postexposure prophylaxis [off-label]**† in adults who are immunocompromised or have chronic liver disease and who have been exposed to HAV within the past 2 weeks and have not completed the hepatitis A vaccination series, a single dose of monovalent hepatitis A vaccine (Havrix®, Vaqta®) along with immune globulin should be administered as soon as possible after exposure.[210,] Administer the vaccine and immune globulin at different injection sites.[210,] When the dose of hepatitis A vaccine administered for postexposure prophylaxis is the first dose the exposed individual has received, a second dose should be administered 6 months after the first dose for long-term immunity; however, the second dose is not required for postexposure prophylaxis.[210,]

The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171,] Consult ACIP for dosage recommendations for human immune globulin when indicated for postexposure prophylaxis against HAV infection.[210,]

The fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) should not be used for HAV postexposure prophylaxis since this vaccine contains less HAV antigen.[210,]

Pediatric Patients

Primary Immunization Against HAV Infection.

The American Academy of Pediatrics (AAP) and other organizations recommend hepatitis A vaccination in children at 12—23 months of age, with a 2-dose series of the monovalent hepatitis A vaccine (Havrix®, Vaqta®) administered with a minimal interval of 6 months; the timing of the second dose is dependent on the vaccine product used.[210,214,304,] Catch-up vaccination is recommended for unvaccinated children and adolescents 2–18 years of age with a 2-dose series of the vaccine administered with a minimal interval of 6 months.[210,214,304,] Persons who previously received 1 dose at 12 months of age or older should receive the second dose ≥6 months after the first dose.[214,304,]

If Havrix® is used for primary immunization in children and adolescents 12 months to 18 years of age, the manufacturer states that an initial dose of the age-appropriate preparation should be given followed by a second (booster) dose 6–12 months after the initial dose.[1,] Children and adolescents 12 months through 18 years of age shoulc receive 720-unit doses; each dose is 0.5 mL.[1,]

If Vaqta® is used for primary immunization in children and adolescents 12 months to 18 years of age, the manufacturer states that an initial dose of the age-appropriate preparation should be given followed by a second (booster) dose 6–18 months after the initial dose.[171,] Children and adolescents 12 months through 18 years of age should receive 25-unit doses; each dose is 0.5 mL.[171,] If Havrix® was used for the primary dose, the manufacturer states that a booster dose of Vaqta® may be given at 6–12 months following the primary dose.[171,]

Preexposure Vaccination Against HAV Infection in High-risk Groups (International Travel).

The ACIP and AAP recommend hepatitis A vaccination (with the monovalent hepatitis A vaccine [Havrix®, Vaqta®]) in susceptible children and adolescents (i.e., unvaccinated, partially vaccinated, or never infected) traveling to or working in countries with high or intermediate endemic HAV since these individuals are at increased risk of HAV infection.[210,214,304,]

In **infants 6–11 months of age [off-label]**†, 1 dose of the vaccine is recommended before departure, with revaccination (i.e., routine primary immunization) with 2 doses separated by ≥6 months at 12—23 months of age.[210,214,304]

In unvaccinated, healthy children and adolescents ≥12 months of age, 1 dose of the vaccine should be administered as soon as travel is considered, and the vaccine series should be completed according to routine schedule.[210,214,304]

For children and adolescents ≥12 months of age with immunocompromising conditions or with chronic liver disease, ACIP recommends that 1 dose of the vaccine be administered as soon as travel is considered.[210] Individuals traveling in <2 weeks should receive the initial dose of the vaccine and may be administered immune globulin concurrently at a different injection site.[210] The hepatitis A vaccine series should be completed according to routine schedule.[210] Consult ACIP guidelines for dosage recommendations for immune globulin.[210]

The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171]

Outbreak Control.

In the setting of an HAV outbreak, ACIP recommends a single dose of the monovalent hepatitis A vaccine (Havrix®, Vaqta®) in all unvaccinated persons ≥1 year of age who are at risk for HAV infection or at risk for severe disease from HAV.[210] A single dose of preexposure hepatitis A vaccine has been shown to successfully control HAV outbreaks.[210] The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171]

Postexposure Prophylaxis of HAV Infection.

For **postexposure prophylaxis [off-label]**† in healthy individuals ≥12 months of age exposed to HAV within the past 2 weeks and who have not completed the hepatitis A vaccination series, a single dose of monovalent hepatitis A vaccine (Havrix®, Vaqta®) should be administered as soon as possible.[210] When the dose of hepatitis A vaccine administered for postexposure prophylaxis is the first dose the exposed individual has received, a second dose should be administered 6 months after the first dose for long-term immunity; however, the second dose is not required for postexposure prophylaxis.[210]

For **postexposure prophylaxis [off-label]**† in individuals (≥12 months of age) who are immunocompromised or have chronic liver disease, who have been exposed to HAV within the past 2 weeks, and have not completed the hepatitis A vaccination series, a single dose of monovalent hepatitis A vaccine (Havrix®, Vaqta®) along with immune globulin should be administered as soon as possible after exposure.[210] Administer the vaccine and immune globulin at different injection sites.[210] When the dose of hepatitis A vaccine administered for postexposure prophylaxis is the first dose the exposed individual has received, a second dose should be administered 6 months after the first dose for long-term immunity; however, the second dose is not required for postexposure prophylaxis.[210] Consult ACIP for dosage recommendations for immune globulin for postexposure prophylaxis against HAV infection.[210]

The age-appropriate preparation of Havrix® or Vaqta® should be administered.[1,171]

▪ Special Populations

Hepatic Impairment

The manufacturers make no specific dosage recommendations for patients with hepatic impairment.[1,171,186] However, data suggest that patients with chronic liver disease have a lower antibody response to Havrix® than healthy subjects.[1]

Renal Impairment

The manufacturers make no specific dosage recommendations for patients with renal impairment.[1,171,186]

Geriatric Patients

The manufacturers make no specific dosage recommendations for geriatric patients.[1,171,186]

Cautions

▪ Contraindications

Monovalent hepatitis A vaccine (Havrix®, Vaqta®): Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis A-containing vaccine, or to any ingredient in the respective vaccine formulation, including neomycin.[1,171]

Fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®): Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis A- or hepatitis B-containing vaccine, or to any component of Twinrix®, including yeast and neomycin.[186]

▪ Warnings/Precautions

Hypersensitivity Reactions

Appropriate medical equipment and supervision should be available for immediate treatment if an anaphylactic reaction occurs following administration of the vaccine.[1,171,186]

Prior to vaccine administration, the clinician should review the patient's immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions to allow an assessment of benefits and risks of administration.[186]

Latex Hypersensitivity

The vial stopper of Vaqta® contains dry natural latex that may cause hypersensitivity reactions in latex-sensitive individuals.[171]

Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines.[1,186] Syncope can be accompanied by transient neurological signs (e.g., visual disturbance, paresthesia, tonic-clonic limb movements).[1,186]

Ensure procedures are in place to avoid a fall injury and to restore cerebral perfusion following syncope.[1,186]

Individuals with Altered Immunocompetence

Individuals who are immunocompromised (including those on immunosuppressant therapy) may have a diminished immune response to the vaccine.[1,171,186,210]

Consult the US Public Health Service Advisory Committee on Immunization Practices (ACIP) for specific information on hepatitis A vaccination in individuals with altered immunocompetence (e.g., individuals with human immunodeficiency virus, hematopoietic cell transplant recipients) or individuals receiving immunosuppressant therapy (e.g., chemotherapy).[210]

Multiple Sclerosis

The manufacturer of Twinrix® states that findings from 2 clinical studies indicate that there is no association between hepatitis B vaccination and the development of multiple sclerosis; vaccination with hepatitis B vaccine does not appear to increase the short-term risk of relapse in individuals with multiple sclerosis.[186]

Limitations of Vaccine Effectiveness

The monovalent hepatitis A vaccines (Havrix® or Vaqta®) provide protection only against hepatitis A virus (HAV).[1,171] The fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) provides protection only against HAV and hepatitis B virus (HBV).[186]

The possibility that unrecognized HAV infection may be present in some individuals at the time of vaccination (since the infection has a long incubation period of 15–50 days) and that hepatitis A vaccine may not prevent infection in such individuals should be considered.[1,171,186] Hepatitis B also has a relatively long incubation period; the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) may also not prevent HBV in individuals who have an unrecognized hepatitis B infection at the time of vaccination.[186]

Vaccination with monovalent hepatitis A vaccines (Havrix® or Vaqta®) or the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) may not protect all individuals.[1,171,186]

Concomitant Illness

The decision whether to administer or delay administration of hepatitis A vaccine or the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine in an individual with a current or recent acute illness depends largely on the severity of symptoms and etiology of the illness.[303] The ACIP states that safety and efficacy of vaccination have been documented in persons who have mild illnesses.[303] However, vaccination of individuals with moderate or severe acute illness generally should be delayed until they have recovered from the acute phase of the illness.[303] This precaution avoids superimposing adverse effects of the vaccine on the underlying illness or mistakenly concluding that a manifestation of the underlying illness resulted from vaccination.[303]

To avoid diagnostic confusion between possible vaccine adverse effects and manifestations of an acute illness, the manufacturer of Twinrix® states that vaccination should be postponed in individuals with moderate or severe acute febrile illness unless they are at immediate risk of hepatitis A or hepatitis B infection.[186]

Individuals with Bleeding Disorders

Hepatitis A vaccine and the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine should be administered with caution to individuals with bleeding disorders (e.g., hemophilia) or individuals receiving anticoagulant therapy, since hematoma may occur following IM administration of the vaccines in such individuals.[303]

ACIP states that a vaccine may be given IM to individuals who have bleeding disorders or are receiving anticoagulant therapy if a clinician familiar with the patient's bleeding risk determines that the vaccine can be administered with reasonable safety.[303] In these cases, a fine needle (23 gauge or smaller) should be used to administer the vaccine and firm pressure should be applied to the injection site (without rubbing) for ≥2 minutes.[303] In individuals with a bleeding disorder who are receiving antihemophilic factor or other similar therapy, IM vaccination can be scheduled shortly after a dose of such therapy to minimize the risk of bleeding.[303] The individual and/or their family should be instructed concerning the risk of hematoma from the injection.[303]

Interference with Laboratory Tests

The manufacturer of Twinrix® states that hepatitis B surface antigen (HBsAg) derived from hepatitis B vaccines may be transiently present in blood samples following vaccination.[186] Serum HBsAg detection may lack diagnostic significance within 28 days of receipt of a hepatitis B vaccine, including Twinrix®.[186]

Use of Fixed Combinations

Whenever the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) is used, the contraindications and precautions related to both antigens should be considered.[186]

Specific Populations

Pregnancy.

Monovalent hepatitis A vaccine (Havrix®, Vaqta®): There are no adequate and well-controlled studies of monovalent hepatitis A vaccine in pregnant women.[1,171] Available data do not suggest an increased risk of major birth defects or miscarriage in pregnant women who received the vaccine.[1,171] No animal studies have been conducted with the vaccine.[1,171]

Fixed-combination vaccine containing HAV vaccine and HBV vaccine (HepA-HepB; Twinrix®): There are no adequate and well-controlled studies of the vaccine in pregnant women.[186] Available data do not suggest an increased risk of major birth defects or miscarriage in pregnant women who received the vaccine within 28 days prior to conception or during pregnancy.[186] In a developmental toxicity study in female rats administered the vaccine prior to mating and during gestation (0.2 mL at each

occasion), no adverse effects on fetal or pre-weaning development were observed.[186,]

ACIP states that data on the administration of the hepatitis A vaccine during pregnancy remain limited.[210,] However, a published safety review of 139 reports submitted to the Vaccine Adverse Event Reporting System (VAERS) between 1996 and 2013 involving pregnant women who received either the hepatitis A vaccine or the combination HepA-HepB (Twinrix®) vaccine did not reveal any concerning patterns of adverse events in either the pregnant individuals or their infants.[210,] Additionally, a multisite study conducted through the CDC's Vaccine Safety Datalink— a population-based research and surveillance system— found no association between maternal hepatitis A vaccination and an increased risk of adverse outcomes among pregnancies resulting in live births.[210,]

ACIP recommends that pregnant women identified as being at risk for HAV infection (e.g., international travelers, individuals who use injection or non-injection drugs [i.e., illegal drug users], those with occupational exposure risks, individuals expecting close contact with an international adoptee, individuals experiencing homelessness) or who are at increased risk for severe outcomes from HAV infection (e.g., individuals with chronic liver disease or human immunodeficiency virus infection) should receive the hepatitis A vaccine during pregnancy if they have not been previously vaccinated.[210,]

CDC states that pregnant women receive hepatitis A vaccination for the same indications as nonpregnant women.[210,] Unvaccinated or partially vaccinated pregnant adolescents should receive catch-up vaccination.[210,] Pregnant women at risk for HAV infection during pregnancy should receive counseling regarding prevention methods (e.g., hand hygiene) to prevent infection.[210,]

Lactation.

Monovalent hepatitis A vaccine (Havrix®, Vaqta®) and fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®): It is not known whether the vaccine is distributed into human milk.[1,171,186,] Data are not available to assess the effects of the vaccine on the breast-fed child or on milk production.[1,171,186,]

The manufacturers state that the benefits of breast-feeding and the importance of hepatitis A vaccine to the woman should be considered along with the potential adverse effects on the breast-fed child from the vaccine or from the underlying maternal condition.[1,171,186,]

Pediatric Use.

Safety and efficacy of monovalent hepatitis A vaccine (Havrix®, Vaqta®) have not been established in infants younger than 12 months of age.[1,171,]

Safety and efficacy of the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) have not been established in children younger than 18 years of age.[186,]

Geriatric Use.

Clinical studies of Havrix® did not include sufficient numbers of patients 65 years of age or older to determine whether geriatric patients respond differently from younger patients; however, other clinical experience has revealed no evidence of age-related differences.[1,]

Postmarketing safety studies evaluating Vaqta® have included 4769 individuals 65 years of age or older, including 1073 who were 75 years of age or older.[171,] Although no overall differences in immunogenicity or safety were observed between geriatric and younger patients, and other clinical experience revealed no evidence of age-related differences, the possibility that some older patients may exhibit increased sensitivity to the vaccine cannot be ruled out.[171,]

Clinical studies of the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) did not include sufficient numbers of individuals 65 years of age or older to determine whether geriatric individuals respond differently than younger adults.[186,]

Hepatic Impairment.

Following the initial dose, immunogenicity of hepatitis A vaccine (Havrix®) in adults with chronic liver disease of various etiologies (e.g., chronic HBV, chronic hepatitis C virus, moderate chronic liver disease, alcoholic cirrhosis, autoimmune hepatitis, chronic hepatitis/cryptogenic cirrhosis, hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis) was lower than in healthy subjects.[1,] However, 1 month after the second (booster) dose at month 6, seroconversion rates were similar among both groups.[1,] Relevance of these data to the duration of protection afforded by hepatitis A vaccine (Havrix®) is unknown.[1,]

Renal Impairment.

Pharmacokinetics have not been evaluated in patients with renal impairment.[1,171,186,]

▪ Common Adverse Effects

Havrix®: In studies of adults and children ≥2 years of age, the most frequently reported solicited adverse effects were injection-site soreness and headache.[1,]

In studies of children 11–25 months of age, the most frequently reported solicited local reactions were pain and redness, and the frequently reported solicited general adverse reactions were irritability, drowsiness, and loss of appetite.[1,]

Vaqta®: In studies of children 12–23 months of age, the most frequently reported local and systemic adverse effects when the vaccine was administered alone or concomitantly were pain, tenderness, and erythema at the injection site, and fever.[171,]

In studies of children and adolescents 2–18 years of age, the most frequently reported adverse effect when the vaccine was administered alone or concomitantly was pain at the injection site.[171,]

In studies of adults ≥19 years of age, the most frequently reported local and systemic adverse effects when the vaccine was administered alone or concomitantly were pain, tenderness, soreness, or warmth at the injection site, and headache.[171,]

Twinrix®: The most frequently reported local and systemic adverse effects following any dose of the vaccine were soreness and redness at the injection site; headache, and fatigue.[186,]

Drug Interactions

▪ Immune Globulin

Although the geometric mean concentrations in adults who received both immune globulin and the hepatitis A vaccine were lower 1 month after completing the vaccination series compared to those who received the vaccine alone, the proportion of adults who ultimately achieved protective antibody levels was not substantially different.[210,]

Monovalent hepatitis A vaccine (Havrix®, Vaqta®) and the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) may be administered concomitantly with immune globulin when indicated for preexposure or postexposure prophylaxis against HAV.[1,171,186,210,]

The manufacturers and the US Public Health Service Advisory Committee on Immunization Practices (ACIP) states that, if combined active immunization with hepatitis A vaccine and passive immunization with immune globulin is used, the vaccine should be administered concurrently with immune globulin using different syringes and different injection sites.[1,171,186,210,] Do not mix the hepatitis A vaccine with any product.[1,186,]

▪ Immunosuppressive Agents

Individuals receiving immunosuppressive therapy (e.g., alkylating agents, antimetabolites, corticosteroids [at greater than physiological dosages], cytotoxic agents, radiation) may have a reduced immune response to hepatitis A vaccination.[1,171,186,]

Consult CDC/ACIP recommendations for specific guidance for hepatitis A vaccination in individuals receiving immunosuppressive therapy.[210,303,]

▪ Vaccines

Hepatitis A vaccine may be given simultaneously with other age-appropriate vaccines during the same health-care visit using different syringes and injection sites.[1,171,210,] Do not mix the hepatitis A vaccine with any other vaccine in the same syringe or vial.[1,171,186,]

Data are not available to date regarding concomitant administration of the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) and other vaccines.[186,]

Diphtheria and Tetanus Toxoids and Pertussis Vaccines

Havrix® was administered concurrently with diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed (DTaP; Infanrix®) and Haemophilus influenzae type b (Hib) polysaccharide conjugate (tetanus toxoid conjugate) vaccine in children starting at 15 months of age.[1,] There was no evidence for reduced antibody response to diphtheria and tetanus toxoids, pertussis, or Hib when Havrix® was administered concomitantly with DTaP and Hib conjugate vaccine relative to DTaP and Hib conjugate vaccine administered together.[1,]

Vaqta® has been administered concomitantly with DTaP (Tripedia®) in children 18 months of age.[171,] Seropositivity rates for diphtheria and tetanus were similar to those observed in historical controls; however, data were insufficient to assess the pertussis response of DTaP when administered concomitantly with Vaqta®.[171,] Rates of seroprotection to hepatitis A were similar between children who received Vaqta® with or without DTaP.[171,]

Vaqta® has been administered concomitantly with DTaP (Infanrix®) and Hib conjugate vaccine (PedvaxHIB®) in children 15 months of age.[171,] When the first dose of Vaqta® was administered concomitantly with either DTaP plus Hib vaccines or Hib vaccine, no interference in immune response to hepatitis A was observed as measured by seropositivity rates after the second dose of Vaqta® compared to administration of both doses of Vaqta® alone.[171,] When the first dose of Vaqta® was administered concomitantly with either DTaP plus Hib vaccines or Hib vaccine, there was no interference in immune response to Haemophilus influenzae type b, compared to individuals receiving either DTaP plus Hib vaccines or Hib vaccine.[171,] When Vaqta® was administered concomitantly with DTaP plus Hib vaccines, there was no interference in immune responses at 4 weeks after vaccination to the pertussis antigens and no interference in immune responses to diphtheria or tetanus toxoid compared to administration of DTaP plus Hib vaccine.[171,]

Haemophilus Influenza Type b (Hib) Vaccine

Havrix® was administered concurrently with Hib polysaccharide conjugate (tetanus toxoid conjugate) vaccine and DTaP (Infanrix®) in children starting at 15 months of age.[1,] There was no evidence for reduced antibody response to diphtheria and tetanus toxoids, pertussis, or Hib when Havrix® was administered concomitantly with DTaP and Hib conjugate vaccine relative to DTaP and Hib conjugate vaccine administered together.[1,]

Vaqta® has been administered concomitantly with Hib conjugate vaccine (PedvaxHIB®) and DTaP (Infanrix®) in children 15 months of age.[171,] When the first dose of Vaqta® was administered concomitantly with either DTaP plus Hib vaccines or Hib vaccine, no interference in immune response to hepatitis A was observed as measured by seropositivity rates after the second dose of Vaqta® compared to administration of both doses of Vaqta® alone.[171,] When the first dose of Vaqta® was administered concomitantly with either DTaP plus Hib vaccines or Hib vaccine, there was no interference in immune response to Haemophilus influenzae type b, compared to individuals receiving either DTaP plus Hib vaccines or Hib vaccine.[171,] When Vaqta® was administered concomitantly with DTaP plus Hib vaccines, there was no interference in immune responses at 4 weeks after vaccination to the pertussis antigens and no interference in immune responses to diphtheria or tetanus toxoid compared to administration of DTaP plus Hib vaccine.[171,]

Hepatitis B Vaccine

Studies have shown that monovalent hepatitis A vaccine and monovalent hepatitis B vaccine can be administered simultaneously at different sites without interfering with the immune response or increasing the frequency of adverse effects to either vaccine.[210,]

Studies in adults indicate that immune responses and adverse effects reported in individuals who received a 3-dose series of the fixed-combination vaccine containing hepatitis A vaccine and hepatitis B vaccine (HepA-HepB; Twinrix®) are similar to those reported in individuals who received a 2-dose series of monovalent hepatitis A vaccine (Havrix®) and a 3-dose series of monovalent hepatitis B vaccine (Engerix-B®) given concurrently in opposite arms.[186,]

Measles, Mumps, and Rubella Virus Vaccine Live

Havrix® was administered concurrently with measles, mumps, and rubella virus vaccine live (MMR) and varicella vaccine in children 15 months of age in a US multicenter study.[1,] There was no evidence for interference in the immune response to MMR and varicella vaccines when administered concomitantly with Havrix® relative to the response when the vaccines were administered without Havrix®.[1,]

In a study involving children 12 months of age who received the first dose of Vaqta® concurrently with MMR (MMR®II) and varicella (Varivax®) vaccines, the seroprotection rates against hepatitis A were comparable between those who received Vaqta® alone and those who received Vaqta® concurrently with MMR and varicella vaccines.[171,] Seropositivity rates were 98.8% for measles, 99.6% for mumps, and 100% for rubella, aligning with historical data observed following administration of the first dose of MMR in this age group.[171,]

Pneumococcal Vaccine

Concomitant administration of pneumococcal 7-valent conjugate vaccine (PCV7; Prevnar®) and Havrix® hepatitis A vaccine in children 15 months of age did not affect the immune response to either vaccine.[1,]

In a clinical trial evaluating the concomitant administration of Vaqta® with PCV7 (Prevnar®) and the MMR-varicella vaccine (ProQuad®) in children 12–15 months of age, the geometric mean antibody titers (GMTs) for *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F measured 6 weeks post-vaccination were non-inferior in individuals who received all 3 vaccines compared to those who received PCV7 and MMR-varicella vaccines alone.[171,] Hepatitis A immune responses were comparable between the 2 groups receiving Vaqta® with or without concomitant PCV7 and MMR-varicella vaccine.[171,] Additionally, seroconversion rates and antibody titers for varicella and the specified *S. pneumoniae* serotypes were similar between groups at 6 weeks after vaccination.[171,]

Poliovirus Vaccine

Available data are insufficient to evaluate the immune response to Vaqta® and poliovirus vaccine when administered concurrently.[171,]

Varicella Virus Vaccine Live

Havrix® was administered concurrently with measles, mumps, and rubella virus vaccine live (MMR) and varicella vaccine in children 15 months of age in a US multicenter study.[1,] There was no evidence for interference in the immune response to MMR and varicella vaccines when administered concomitantly with Havrix® relative to the response when the vaccines were administered without Havrix®.[1,]

In a clinical trial involving children 12 months of age who received the first dose of Vaqta® concurrently with MMR and varicella (Varivax®) vaccines, the seroprotection rates against hepatitis A were comparable between those who received Vaqta® alone and those who received Vaqta® concurrently with MMR and varicella vaccines.[171,] However, immunogenicity data from this study are insufficient to assess the response to the varicella vaccine.[171,]

Typhoid and Yellow Fever Vaccines

In a study evaluating the concomitant administration of Vaqta® with typhoid Vi polysaccharide vaccine (Typhim Vi®) and yellow fever vaccine in adults 18–54 years of age, antibody response rates to the typhoid and yellow fever vaccines were adequate when these vaccines were administered both with and without Vaqta®.[171,] The seropositivity rate for hepatitis A was generally comparable between individuals who received Vaqta® in combination with the typhoid and yellow fever vaccines and those who received Vaqta® alone.[171,]

Description

Hepatitis A virus (HAV) vaccine is an inactivated vaccine that contains cell culture-adapted, inactivated HAV.[1,171,186,210,] Hepatitis A virus vaccine is commercially available in the US as monovalent (single-antigen) vaccines (Havrix®, Vaqta®)[1,171,] and in a fixed-combination vaccine with hepatitis B vaccine (HepA-HepB; Twinrix®).[186,]

Hepatitis A virus, a member of the picornavirus family, is one of multiple hepatitis viruses capable of causing systemic illness with primary hepatic involvement.[1,] The average incubation period for HAV is approximately 28 days (range, 15–50 days).[1,] The clinical presentation of HAV infection is highly variable, ranging from asymptomatic infection to symptomatic icteric hepatitis and, in rare cases, death.[1,186,] Hepatitis A vaccines stimulate active immunity to HAV infection by inducing production of antibodies to hepatitis A.[171,] The presence of anti-HAV antibodies is indicative of immunity and provides protection against subsequent HAV infection; however, the lowest titer required to confer immunity has not yet been clearly established.[1,171,186,] Natural infection provides lifelong immunity even when anti-HAV antibodies are undetectable.[186,] Infection with hepatitis B virus (HBV) can lead to serious health outcomes such as acute massive hepatic necrosis and chronic active hepatitis.[186,] Individuals with chronic HBV infection have an increased risk of developing cirrhosis and hepatocellular carcinoma.[186,]

Havrix® is a sterile, inactivated viral suspension derived from the HM175 strain of the HAV, which is cultured in MRC-5 human diploid cells.[1,] Following the removal of the culture medium, the cells are lysed to produce a viral suspension.[1,] This suspension undergoes purification through ultrafiltration and gel permeation chromatography.[1,] The resulting lysate is treated with formalin to inactivate the virus.[1,] The viral antigen content is quantified using a standardized enzyme-linked immunosorbent assay (ELISA) and is expressed in ELISA Units (ELU).[1,] Each 1-mL adult dose contains 1440 ELU of viral antigen adsorbed onto 0.5 mg of aluminum in the form of aluminum hydroxide.[1,] Each 0.5-mL pediatric dose contains 720 ELU of viral antigen adsorbed onto 0.25 mg of aluminum as aluminum hydroxide.[1,]

Vaqta® is a sterile, inactivated whole-virus vaccine developed from the CR326F strain of the HAV, which is propagated in human MRC-5 diploid fibroblast cell cultures.[171] The vaccine contains an inactivated viral strain that has been further attenuated through serial passage from an established attenuated strain.[171,] The virus is cultivated, harvested, and purified using a combination of physical methods and high-performance liquid chromatography techniques.[171,] It is then inactivated with formalin and adsorbed onto amorphous aluminum hydroxyphosphate sulfate.[171,] Each 1-mL adult dose of Vaqta® vaccine contains approximately 50 units of viral antigen, 0.45 mg of

aluminum (as amorphous aluminum hydroxyphosphate sulfate), and 70 mcg of sodium borate as a pH stabilizer, in 0.9% sodium chloride.[171,] Each 0.5-mL pediatric dose of Vaqta® vaccine contains approximately 25 units of viral antigen, 0.225 mg of aluminum (as amorphous aluminum hydroxyphosphate sulfate), and 35 mcg of sodium borate, in 0.9% sodium chloride.[171,]

Hepatitis A virus vaccine inactivated and hepatitis B vaccine (recombinant) is a fixed-combination vaccine that contains both HAV and hepatitis B virus (HBV) antigens.[186] The commercially available fixed-combination vaccine (HepA-HepB; Twinrix®) is a sterile suspension containing the antigenic components used to produce Havrix® hepatitis A vaccine and Engerix-B® hepatitis B vaccine.[186,] Twinrix® is a sterile suspension comprising inactivated HAV (strain HM175) and noninfectious hepatitis B surface antigen (HBsAg).[186,] The HAV is cultivated in MRC-5 human diploid cells and subsequently inactivated using formalin.[186,] The HBsAg component is produced through the culture of genetically engineered *Saccharomyces cerevisiae* (yeast) cells that express the surface antigen gene of the HBV.[186,] Each antigenic component is adsorbed separately onto aluminum phosphate or aluminum hydroxide and then pooled to form the fixed-combination preparation.[186,] Each 1-mL dose of Twinrix® contains 720 units of hepatitis A viral antigen and 20 mcg of HBsAg and also contains 0.45 mg of aluminum (as aluminum hydroxide and aluminum phosphate).[186,]

While the absolute minimum concentration of anti-HAV antibodies required to prevent HAV infection has not been definitively established, it is likely to be very low.[210,] The levels of anti-HAV achieved through active immunization via vaccination are typically 10–100 times lower than those observed following natural infection.[210,] Due to the absence of a clearly defined protective threshold, the lower limit of detection of the specific assay employed is generally considered the protective level.[210,] In post-vaccination studies, a concentration of ≥10 mIU/mL is used as the minimum protective level.[210,]

Hepatitis A vaccination can lead to the transient appearance of immunoglobulin M (IgM) anti-HAV antibodies, particularly when testing is conducted within a few weeks after vaccination.[210,] IgM anti-HAV has been detected in 8–20% of adults approximately 2–3 weeks following administration of a single vaccine dose.[210,] Lifelong protection might occur after hepatitis A vaccination; however, the exact duration of protection from HAV infection following administration of the vaccines has not been fully defined.[210,] Although there is evidence of waning anti-HAV antibody levels over time, the presence of an anamnestic response following administration of hepatitis A vaccine booster doses suggests sustained immune memory and continued protection against HAV infection.[210,] Additionally, cellular immune responses may also play a role in maintaining long-term immunity.[210,]

Advice to Patients

The following information contains important points for the clinician to discuss with patients during counseling. For more comprehensive monographs suitable for distribution to the patient, please refer to the *AHFS Patient Medication Information* monographs available from MedlinePlus (https://vsearch.nlm.nih.gov/vivisimo/cgi-bin/query-meta?v:project=medlineplus) (in English and Spanish; written at a 6th- to 8th-grade reading level).

- Prior to administration of the hepatitis A (HepA) vaccine, provide a copy of the manufacturer's patient information to the patient and/or patient's parent or guardian.[1,171,186,] Prior to administration of each vaccine dose, also provide a copy of the appropriate Centers for Disease Control and Prevention (CDC) Vaccine Information Statement (VIS) to the patient or patient's legal representative as required by the National Childhood Vaccine Injury Act (VISs are available at https://www.cdc.gov/vaccines/hcp/current-vis/hepatitis-a.html (https://www.cdc.gov/vaccines/hcp/current-vis/hepatitis-a.html)).[1,171,186,202,]
- Advise the patient and/or patient's parent or guardian of the risks and benefits of vaccination with HepA vaccine.[1,171,186,]
- Advise patient and/or patient's parent or guardian that HepA vaccines do not contain live viruses and cannot cause hepatitis infection.[1,171,186,]
- Advise the patient and/or patient's parent or guardian of the importance of receiving both the initial dose and second (booster) dose to ensure the highest level of protection against hepatitis A virus.[1,171,186,]
- Advise the patient and/or patient's parent or guardian to inform clinicians if any adverse reactions (e.g., hypersensitivity reactions) occur.[1,171,186,] Clinicians or individuals can report any adverse reactions that occur following vaccination to the Vaccine Adverse Event Reporting System (VAERS) at 800-822-7967 or https://vaers.hhs.gov/index.html (https://vaers.hhs.gov/index.html) .[1,171,186,]
- Advise patients to inform their clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as any concomitant illnesses.[1,171,186,]
- Advise patients to inform clinicians if they are or plan to become pregnant or plan to breast-feed.[1,171,186,]
- Advise patients of other important precautionary information.[1,171,186,]

Additional Information

The American Society of Health-System Pharmacists, Inc. represents that the information provided in the accompanying monograph was formulated with a reasonable standard of care, and in conformity with professional standards in the field. Readers are advised that decisions regarding use of drugs are complex medical decisions requiring the independent, informed decision of an appropriate health care professional, and that the information contained in the monograph is provided for informational purposes only. The manufacturer's labeling should be consulted for more detailed information. The American Society of Health-System Pharmacists, Inc. does not endorse or recommend the use of any drug. The information contained in the monograph is not a substitute for medical care.

Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Hepatitis A Virus Vaccine Inactivated (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=NonProprietaryName&ApptName=Hepatitis+A+Virus+Vaccine+Inactivated&collapse=1)

Parenteral

Injectable suspension, for IM use

25 units (of viral antigen) per 0.5 mL

Vaqta® Pediatric/Adolescent, Merck (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=LabelerName&ApptName=Merck&collapse=1)

50 units (of viral antigen) per mL

Vaqta® Adult, Merck (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=LabelerName&ApptName=Merck&collapse=1)

720 ELISA units (of viral antigen) per 0.5 mL

Havrix® Pediatric, GlaxoSmithKline (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=LabelerName&ApptName=GlaxoSmithKline&collapse=1)

1440 ELISA units (of viral antigen) per mL

Havrix® Adult, GlaxoSmithKline (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=LabelerName&ApptName=GlaxoSmithKline&collapse=1)

Hepatitis A Inactivated and Hepatitis B (Recombinant) Vaccine (HepA-HepB) (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=NonProprietaryName&ApptName=Hepatitis+A+Inactivated+and+Hepatitis+B+%28Recombinant%29+Vaccine+%28HepA-HepB%29&collapse=1)

Parenteral

Injectable suspension, for IM use

Hepatitis A Virus Vaccine Inactivated 720 ELISA units (of viral antigen) and Hepatitis B Vaccine (Recombinant) 20 mcg (of hepatitis B surface antigen) per mL

Twinrix®, GlaxoSmithKline (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=LabelerName&ApptName=GlaxoSmithKline&collapse=1)

Related Resources

AHFS Patient Medication Information (https://vsearch.nlm.nih.gov/vivisimo/cgi-bin/query-meta?v:project=medlineplus&query=Hepatitis%20A%20Vaccine%20Inactivated) and other related patient health topics (MedlinePlus)
ASHP Drug Shortages Resource Center (https://www.ashp.org/Drug-Shortages)
CCRIS (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+ccris:%%22Hepatitis%20A%20Vaccine%20Inactivated%%22) (Chemical Carcinogenesis Research Information System)
ChemID*plus* (https://chem.nlm.nih.gov/chemidplus/name/Hepatitis%20A%20Vaccine%20Inactivated)
Biochemical Data Summary (http://www.drugbank.ca/unearth/q?utf8=%%E2%%9C%%93&query=Hepatitis%20A%20Vaccine%20Inactivated&searcher=drugs&approved=1&vet_approved=1&nutraceutical=1&illicit=1&withdra
(US and Canada)
Clinical Trials (https://www.clinicaltrials.gov/ct/search?submit=Search&term=Hepatitis%20A%20Vaccine%20Inactivated)
DailyMed (https://dailymed.nlm.nih.gov/dailymed/search.cfm?query=Hepatitis%20A%20Vaccine%20Inactivated) (drug labels)
DART (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+dart:%%22Hepatitis%20A%20Vaccine%20Inactivated%%22) (Developmental and Reproductive Toxicology Database)
Drugs@FDA (https://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchType=BasicSearch&SearchTerm=Hepatitis%20A%20Vaccine%20Inactivated) (approval information)
European Medicines Agency (https://www.ema.europa.eu/en/search/search?search_api_views_fulltext=Hepatitis%20A%20Vaccine%20Inactivated)
FDA National Drug Code Directory (https://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm?sugg=NonProprietaryName&ApptName=Hepatitis%20A%20Vaccine%20Inactivated&collapse=1)
FDA Recalls, Market Withdrawals, and Safety Alerts (https://www.fda.gov/Safety/Recalls/default.htm)
HSDB (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:%%22Hepatitis%20A%20Vaccine%20Inactivated%%22) (Hazardous Substances Data Bank)
Inxight Drugs (https://drugs.ncats.io/substances?q=%%22Hepatitis%20A%20Vaccine%20Inactivated%%22) (National Center for Advancing Translational Sciences)
LactMed (drug effects on breastfeeding) (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+lactmed:@or+%%28@na+%%22Hepatitis%20A%20Vaccine%20Inactivated%%22+%%29)
New Drug Approvals (https://ahfs.ashp.org/drug-assignments.aspx)
Orange Book (https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?panel=0&drugname=Hepatitis%20A%20Vaccine%20Inactivated) (therapeutic equivalence)
PharmGKB (https://www.pharmgkb.org/search?connections&gaSearch=Hepatitis%20A%20Vaccine%20Inactivated&query=Hepatitis%20A%20Vaccine%20Inactivated&type=chemical) (Pharmacogenomic data from PharmGKB)
Pillbox (*beta*) (https://pillbox.nlm.nih.gov/pillimage/search_results.php?submit=Search&splid=&getingredient=Hepatitis%20A%20Vaccine%20Inactivated) (drug identification and images)
PubMed (https://www.ncbi.nlm.nih.gov/pubmed?DB=pubmed&term=Hepatitis%20A%20Vaccine%20Inactivated%%5BAll+Fields%%5D) (scientific journals)
Safety-related Labeling Changes (https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges) (FDA/CDER)
ToxLine (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+toxline:%%22Hepatitis%20A%20Vaccine%20Inactivated%%22) (Toxicology Literature Online)

† Use is not currently included in the labeling approved by the US Food and Drug Administration.

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About ASHP
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Contact Us
ASHP
4500 East-West Highway, Suite 900
Bethesda, Maryland 20814

Customer Service
1-866-279-0681
custserv@ashp.org (mailto:custserv@ashp.org)
softwaresupport@ashp.org (mailto:softwaresupport@ashp.org)

(https://itunes.apple.com/us/app/ahfs-clinical-drug-information/id1068281731)