

PRESCRIBING INFORMATION

TWINRIX®

[Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine]

DESCRIPTION

TWINRIX® [Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine] is a sterile bivalent vaccine containing the antigenic components used in producing HAVRIX® (Hepatitis A Vaccine, Inactivated) and ENGERIX-B® [Hepatitis B Vaccine (Recombinant)]. TWINRIX is a sterile suspension of inactivated hepatitis A virus (strain HM175) propagated in MRC₅ cells, and combined with purified surface antigen of the hepatitis B virus. The purified hepatitis B surface antigen (HBsAg) is obtained by culturing genetically engineered *Saccharomyces cerevisiae* cells, which carry the surface antigen gene of the hepatitis B virus, in synthetic media containing inorganic salts, amino acids, dextrose, and vitamins. Bulk preparations of each antigen are adsorbed separately onto aluminum salts and then pooled during formulation.

A 1.0-mL dose of vaccine contains not less than 720 ELISA Units of inactivated hepatitis A virus and 20 mcg of recombinant HBsAg protein. One dose of vaccine also contains 0.45 mg of aluminum in the form of aluminum phosphate and aluminum hydroxide as adjuvants, amino acids, 5.0 mg 2-phenoxyethanol as a preservative, sodium chloride, phosphate buffer, polysorbate 20, Water for Injection, traces of formalin (not more than 0.1 mg), a trace amount of thimerosal (<1 mcg mercury) from the manufacturing process, and residual MRC₅ cellular proteins (not more than 2.5 mcg). Neomycin sulfate, an aminoglycoside antibiotic, is included in the cell growth media; only trace amounts (not more than 20 ng) remain following purification. The manufacturing procedures used to manufacture TWINRIX result in a product that contains no more than 5% yeast protein.

TWINRIX 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.

CLINICAL PHARMACOLOGY

Several hepatitis viruses (A, B, C, D, and E) are known to cause a systemic infection resulting in major pathologic changes in the liver. Features of hepatitis A and hepatitis B are described below.

Hepatitis A: The hepatitis A virus (HAV) belongs to the picornavirus family. Only one serotype of HAV has been described.¹

Hepatitis A is a highly contagious disease with the predominant mode of transmission being person-to-person via the fecal-oral route. Infection has been shown to be spread (1) by contaminated water or food; (2) by infected food handlers²; (3) after breakdown in usual sanitary conditions or after floods or natural disasters; (4) by ingestion of raw or undercooked shellfish (oysters, clams, mussels) from contaminated waters³; (5) during travel to areas of the world with

poor hygienic conditions⁴; (6) among institutionalized children and adults⁵; (7) in day-care centers⁶; and (8) by parenteral transmission, either blood transfusions or sharing needles with infected people.⁷

In the United States, attack rates for hepatitis A disease are cyclical and vary by population. The rates have increased gradually from 10.4 per 100,000 in 1987 to 11.7 per 100,000 in 1996.⁸

The incubation period for hepatitis A averages 28 days (range: 15 to 50 days).⁹ The course of hepatitis A infection is extremely variable, ranging from asymptomatic infection to icteric hepatitis. However, most adults (76% to 97%) become symptomatic.¹⁰ Symptoms range from mild and transient to severe and prolonged, and may include fever, nausea, vomiting, and diarrhea in the prodromal phase, followed by jaundice in up to 88% of adults, as well as hepatomegaly and biochemical evidence of hepatocellular damage.¹⁰ Recovery is generally complete and followed by protection against HAV infection. However, illness may be prolonged, and relapse of clinical illness and viral shedding have been described.¹¹ Up to 22% of adults who contract hepatitis A are hospitalized and approximately 100 patients die annually in the United States from complications of hepatitis A.¹²

Chronic shedding of HAV in feces has not been demonstrated, but relapses of hepatitis A can occur in as many as 20% of patients^{11,13} and fecal shedding of HAV may recur at this time.¹¹ Approximately 70% of pediatric patients less than 6 years of age infected with hepatitis A are asymptomatic, and serve as a reservoir for infection among adults.¹²

The presence of antibodies to HAV, as detected in a standardized assay (HAVAB), is an indication of the presence of protective antibodies against hepatitis A disease. Natural infection provides lifelong immunity even when antibodies to hepatitis A are undetectable. At present, studies show the duration of protection afforded by TWINRIX against hepatitis A lasts at least 4 years.¹⁴

Hepatitis B: The hepatitis B virus (HBV) belongs to a family of genetically related DNA-containing animal viruses, which are hepatotropic. The incubation period of hepatitis B ranges between 30 and 180 days. The mode of transmission of hepatitis B may be: By contact (contaminated body secretions including semen, vaginal secretions, blood, saliva); percutaneously (usually through accidental needlesticks or by sharing needles with infected people); or by maternal-neonatal transmission.¹⁵

HBV infection occurs throughout the world with highly variable prevalences. A human reservoir of persistently infected persons is present in nearly all communities of the world. In the United States, parenteral drug abuse, unprotected sexual activity, occupationally acquired infection, or travelers returning from high prevalence countries may be the principal mechanisms of HBV transmission.

Clinical infection with hepatitis B may occur in 2 major forms: Asymptomatic or symptomatic hepatitis. Asymptomatic HBV infection can be subclinical or inapparent. In subclinical infection, patients have abnormal liver enzymes without jaundice, while inapparent asymptomatic infection is identified only by serological testing. One in 4 adults who has symptomatic disease has jaundice (anicteric/icteric hepatitis).

HBV infection can have serious consequences including acute massive hepatic necrosis, chronic active hepatitis, and cirrhosis of the liver. As many as 90% of infants and 6% to 10% of adults who are infected in the United States will become HBV carriers.¹² An estimated 200 to 300 million people are chronic carriers of HBV worldwide.¹² The Centers for Disease Control and Prevention (CDC) estimates that there are approximately 1 million to 1.25 million chronic carriers of HBV in the United States.¹² About 50,000 cases of hepatitis are reported per year, about half of which are hepatitis B. Unreported cases may be 10 times greater. Close contact (sexual contact or household contact) or exposure to blood from infected individuals is associated with increased risk of infection. Those patients who become chronic carriers can infect others and are at increased risk of developing primary hepatocellular carcinoma. Among other factors, infection with HBV may be the single most important factor for development of this carcinoma.^{12,16}

Reduced Risk of Hepatocellular Carcinoma: A clear link has been demonstrated between chronic HBV infection and the occurrence of hepatocellular carcinoma. In a Taiwanese study, the institution of universal childhood immunization against HBV has been shown to decrease the incidence of hepatocellular carcinoma among children.¹⁷ In a Korean study in adult males, vaccination against HBV has been shown to decrease the incidence of, and risk of, developing hepatocellular carcinoma in adults.¹⁸

There is no definitive treatment for acute HBV infection. However, those who develop antibodies to HBsAg after active infection are protected against subsequent infection. Antibody titers ≥ 10 mIU/mL against HBsAg are recognized as conferring protection against HBV.¹⁹ Seroconversion is defined as an antibody titer ≥ 1 mIU/mL.

Clinical Trials: Immunogenicity in Adults: Sera from 1,551 healthy adult volunteers ages 17 to 70, including 555 male subjects and 996 female subjects, in 11 clinical trials were analyzed following administration of 3 doses of TWINRIX on a 0-, 1-, and 6-month schedule. Seroconversion for antibodies against HAV was elicited in 99.9% of vaccinees, and protective antibodies against HBV were detected in 98.5%, 1 month after completion of the 3-dose series.

Table 1. Immunogenicity in TWINRIX Worldwide Clinical Trials

TWINRIX Dose	N	% Seroconversion for Hepatitis A*	% Seroprotection for Hepatitis B†
1	1587	93.8	30.8
2	1571	98.8	78.2
3	1551	99.9	98.5

* Anti-HAV titer \geq assay cut-off: 20 mIU/mL (HAVAB Test) or 33 mIU/mL (ENZYMUN-TEST®).

† Anti-HBsAg titer ≥ 10 mIU/mL (AUSAB®).

One of the 11 trials was a comparative trial conducted in a US population given either TWINRIX (on a 0-, 1-, and 6-month schedule) or HAVRIX (0- and 6-month schedule) and ENGERIX-B (0-, 1-, and 6-month schedule). The monovalent vaccines were given concurrently

in opposite arms. Of a total of 773 adults (ages 18 to 70 years) enrolled in this trial, an immunogenicity analysis was performed in 533 subjects who completed the study according to protocol. Of these, 264 subjects received TWINRIX and 269 subjects received HAVRIX and ENGERIX-B. Seroconversion against HAV and seroprotection against HBV are shown in Table 2.

Table 2. Percentage of Seroconversion or Seroprotection Rates in the TWINRIX US Clinical Trial

Vaccine	N	Timepoint	% Seroconversion for Hepatitis A* (95% CI)	% Seroprotection for Hepatitis B† (95% CI)
TWINRIX	264	Month 1	91.6	17.9
		Month 2	97.7	61.2
		Month 7	99.6 (97.9-100.0)	95.1 (91.7-97.4)
HAVRIX and ENGERIX-B	269	Month 1	98.1	7.5
		Month 2	98.9	50.4
		Month 7	99.3 (97.3-99.9)	92.2 (88.3-95.1)

* Anti-HAV titer \geq assay cut-off: 33 mIU/mL (ENZYMUN-TEST®).

† Anti-HBsAg titer \geq 10 mIU/mL (AUSAB®).

Since the immune responses to hepatitis A and hepatitis B induced by TWINRIX were non-inferior to the monovalent vaccines, efficacy is expected to be similar to the efficacy for each of the monovalent vaccines (Table 3).

Table 3. Geometric Mean Titers in the TWINRIX US Clinical Trial

Vaccine	N	Timepoint	GMT to Hepatitis A (95% CI)	GMT to Hepatitis B (95% CI)
TWINRIX	263	Month 1	335	8
	259	Month 2	636	23
	264	Month 7	4756 (4152-5448)	2099 (1663-2649)
HAVRIX and ENGERIX-B	268	Month 1	444	6
	269	Month 2	257	18
	269	Month 7	2948 (2638-3294)	1871 (1428-2450)

It was noted that the antibody titers achieved 1 month after the final dose of TWINRIX were higher than titers achieved 1 month after the final dose of HAVRIX in these clinical trials. This may have been due to a difference in the recommended dosage regimens for these 2 vaccines, whereby TWINRIX vaccinees received 3 doses of 720 EL.U. of hepatitis A antigen at 0, 1, and 6 months, whereas HAVRIX vaccinees received 2 doses of 1440 EL.U. of the same antigen (at 0 and 6 months). However, these differences in peak titer have not been shown to be clinically significant.

Two clinical trials involving a total of 129 subjects demonstrated that antibodies to both HAV and HBV persisted for at least 4 years after the first vaccine dose in a 3-dose series of TWINRIX, given on a 0-, 1-, and 6-month schedule. For comparison, after the recommended immunization regimens for HAVRIX and ENGERIX-B, respectively, similar studies involving a total of 114 subjects have shown that seropositivity to HAV and HBV also persists for at least 4 years.

The effect of age on immune response to TWINRIX was studied in 2 trials comparing subjects over 40 years of age (n = 183, mean age = 48 in one trial and n = 72, mean age = 50 in the other) with those ≤40 (n = 191; mean age 32.5). The response to the hepatitis A component of TWINRIX declined slightly with age, but >99% of subjects achieved protective antibody levels in both age groups, and antibody titers were comparable to 2 doses of hepatitis A vaccine alone in age matched controls.

The response to hepatitis B immunization is known to decline in vaccinees over 40 years of age. TWINRIX elicited a seroprotective response to hepatitis B in 97% of younger subjects and 93% to 94% of the older subjects, as compared to 92% of older subjects given hepatitis B vaccine alone. Geometric mean titers elicited by TWINRIX were 2,285 in the younger subjects and 1,890 or 1,038 for the older subjects in the 2 trials. Hepatitis B vaccine alone gave titers of 2,896 in younger subjects and 1,157 in those over 40 years of age.

It has been shown in open randomized clinical trials that combining the hepatitis A antigen with the hepatitis B surface antigen in TWINRIX resulted in comparable anti-HAV or anti-HBsAg titers, relative to vaccination with the individual monovalent vaccines or the concomitant administration of each vaccine in opposite arms.

Immune Response to Simultaneously Administered Vaccines: There have been no studies of concomitant administration of TWINRIX with other vaccines.

INDICATIONS AND USAGE

TWINRIX is indicated for active immunization of persons 18 years of age or older against disease caused by hepatitis A virus and infection by all known subtypes of hepatitis B virus. As with any vaccine, vaccination with TWINRIX may not protect 100% of recipients. As hepatitis D (caused by the delta virus) does not occur in the absence of HBV infection, it can be expected that hepatitis D will also be prevented by vaccination with TWINRIX.

TWINRIX will not prevent hepatitis caused by other agents such as hepatitis C virus, hepatitis E virus, or other pathogens known to infect the liver.

Immunization is recommended for all susceptible persons 18 years of age or older who are, or will be, at risk of exposure to both hepatitis A and hepatitis B viruses, including but not limited to:

- *Travelers:* Persons traveling to areas of high/intermediate endemicity for *both* HAV and HBV (see Table 4) *who are at increased risk of HBV infection due to behavioral or occupational factors.* (See CLINICAL PHARMACOLOGY.)

Table 4. Hepatitis A and Hepatitis B Endemicity by Region

Geographic Region	HAV	HBV
Africa	High	High (most)
Caribbean	High	Intermediate
Central America	High	Intermediate
South America (temperate)	High	Intermediate
South America (tropical)	High	High
South and Southeast Asia*	High	High
Middle East†	High	High
Eastern Europe	Intermediate	Intermediate
Southern Europe	Intermediate	Intermediate
Former Soviet Union	Intermediate	Intermediate

*Japan: Low HAV and intermediate HBV endemicity.

† Israel: Intermediate HBV endemicity.

- *Patients With Chronic Liver Disease*, including:
 - alcoholic cirrhosis
 - chronic hepatitis C
 - autoimmune hepatitis
 - primary biliary cirrhosis
- *Persons at Risk Through Their Work*:
 - Laboratory workers who handle live hepatitis A and hepatitis B virus
 - Police and other personnel who render first-aid or medical assistance
 - Workers who come in contact with feces or sewage
- *Others*:
 - Healthcare personnel who render first-aid or emergency medical assistance.
 - Personnel employed in day-care centers and correctional facilities. Residents of drug and alcohol treatment centers. Staff of hemodialysis units.
 - People living in, or relocating to, areas of high/intermediate endemicity of HAV and who have risk factors for HBV.
 - Men who have sex with men.
 - Persons at increased risk of disease due to their sexual practices.^{20, 21}
 - Patients frequently receiving blood products including persons who have clotting factor disorders (hemophiliacs and other recipients of therapeutic blood products).
 - Military recruits and other military personnel at increased risk for HBV.
 - Users of injectable illicit drugs.
 - Individuals who are at increased risk for HBV infection and who are close household contacts of patients with acute or relapsing hepatitis A and individuals who are at increased risk for HAV infection and who are close household contacts of individuals with acute or chronic hepatitis B infection.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including yeast and neomycin, is a contraindication (see DESCRIPTION). This vaccine is contraindicated in patients with previous hypersensitivity to TWINRIX or monovalent hepatitis A or hepatitis B vaccines.

WARNINGS

There have been rare reports of anaphylaxis/anaphylactoid reactions following routine clinical use of TWINRIX. (See CONTRAINDICATIONS.)

The vial stopper is latex-free. 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.

Hepatitis A and hepatitis B have relatively long incubation periods. The vaccine may not prevent hepatitis A or hepatitis B infection in individuals who have an unrecognized hepatitis A or hepatitis B infection at the time of vaccination. Additionally, it may not prevent infection in individuals who do not achieve protective antibody titers.

PRECAUTIONS

General: As with other vaccines, although a moderate or severe acute illness is sufficient reason to postpone vaccination, minor illnesses such as mild upper respiratory infections with or without low-grade fever are not contraindications.²²

Multiple Sclerosis: Results from 2 clinical studies indicate that there is no association between hepatitis B vaccination and the development of multiple sclerosis,²³ and that vaccination with hepatitis B vaccine does not appear to increase the short-term risk of relapse in multiple sclerosis.²⁴

TWINRIX should be administered with caution to people on anticoagulants, and those with thrombocytopenia or a bleeding disorder since bleeding may occur following intramuscular administration to these subjects.

As with any vaccine, if administered to immunosuppressed persons or persons receiving immunosuppressive therapy, the expected immune response may not be obtained.²⁵

Before the injection of any vaccine, the physician should take all reasonable precautions to prevent allergic or other adverse reactions, including understanding the use of the vaccine concerned, and the nature of the side effects and adverse reactions that may follow its use.

Prior to immunization with any vaccine, the patient's 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 TWINRIX and to allow an assessment of benefits and risks. As with any parenteral vaccine, epinephrine injection (1:1,000) and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

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

Information for Patients: Patients should be informed of the benefits and risks of immunization with TWINRIX, and of the importance of completing the immunization series. As with any vaccine, it is important when a subject returns for the next dose in a series that he or she be questioned concerning the occurrence of any symptoms and/or signs after a previous dose of the same vaccine and that adverse events be reported. 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 1-800-822-7967.²⁶

Carcinogenesis, Mutagenesis, Impairment of Fertility: TWINRIX 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 TWINRIX. It is also not known whether TWINRIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. TWINRIX should be given to a pregnant woman only if clearly indicated (see INDICATIONS AND USAGE).

Pregnancy Exposure Registry: Healthcare providers are encouraged to register pregnant women who receive TWINRIX in the GlaxoSmithKline vaccination pregnancy registry by calling 1-888-825-5249.

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

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

Geriatric Use: Clinical studies of TWINRIX did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ADVERSE REACTIONS

In clinical trials involving the administration of 6,543 doses to 2,299 individuals and during routine clinical use of the vaccine outside the United States, TWINRIX has been generally well tolerated.

Of 773 volunteers who participated in the comparative trial conducted in the United States, 389 subjects received at least 1 dose of TWINRIX and 384 received at least 1 dose each of ENGERIX-B and HAVRIX as separate but simultaneous injections. Solicited adverse events reported following the administration of TWINRIX are shown in Table 5, compared with adverse events reported after administration of ENGERIX-B and HAVRIX.

Table 5. Rate of Adverse Events Reported After Administration of TWINRIX or ENGERIX-B and HAVRIX

Adverse Event	TWINRIX			ENGERIX-B			HAVRIX	
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2
	(N = 385)	(N = 382)	(N = 374)	(N = 382)	(N = 376)	(N = 369)	(N = 382)	(N = 369)
Local	%	%	%	%	%	%	%	%
Soreness	37	35	41	41	25	30	53	47
Redness	8	9	11	6	7	9	7	9
Swelling	4	4	6	3	5	5	5	5
Adverse Event	TWINRIX			ENGERIX-B and HAVRIX				
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3		
	(N = 385)	(N = 382)	(N = 374)	(N = 382)	(N = 376)	(N = 369)		
General	%	%	%	%	%	%		
Headache	22	15	13	19	12	14		
Fatigue	14	13	11	14	9	10		
Diarrhea	5	4	6	5	3	3		
Nausea	4	3	2	7	3	5		
Fever	4	3	2	4	2	4		
Vomiting	1	1	0	1	1	1		

Adverse reactions seen with TWINRIX were similar to those observed after vaccination with the monovalent components. The frequency of solicited adverse events did not increase with successive doses of TWINRIX. Most events reported were considered by the subjects as mild and self-limiting and did not last more than 48 hours.

Among 2,299 subjects in 14 clinical trials, the following adverse experiences were reported to occur within 30 days following vaccination with the frequency shown below.

Incidence 1% to 10% of Injections, Seen in Clinical Trials With TWINRIX:

Local Reactions at Injection Site: Induration.

Respiratory System: Upper respiratory tract infections.

Incidence <1% of Injections, Seen in Clinical Trials With TWINRIX:

Local Reactions at Injection Site: Pruritus, ecchymoses.

Body as a Whole: Sweating, weakness, flushing, influenza-like symptoms.

Cardiovascular System: Syncope.

Gastrointestinal System: Abdominal pain, anorexia, vomiting.

Musculoskeletal System: Arthralgia, myalgia, back pain.

Nervous System: Migraine, paresthesia, vertigo, somnolence, insomnia, irritability, agitation, dizziness.

Respiratory System: Respiratory tract illnesses.

Skin and Appendages: Rash, urticaria, petechiae, erythema.

As with any vaccine, it is possible that expanded routine clinical use of the vaccine could reveal rare adverse events.

Incidence <1% of Injections, Seen in Clinical Trials With HAVRIX^a and/or ENGERIX-B^b:

Body as a Whole: Tingling.^b

Cardiovascular System: Hypotension.^b

Gastrointestinal: Constipation,^b dysgeusia.^a

Hematologic/lymphatic: Lymphadenopathy.^{a+b}

Musculoskeletal System: Elevation of creatine phosphokinase.^a

Nervous System: Hypertonic episode,^a photophobia.^a

Postmarketing Reports With HAVRIX and/or ENGERIX-B: Since market introduction, more than 61 million doses of HAVRIX and more than 600 million doses of ENGERIX-B have been distributed worldwide (circa 2000).²⁷ Voluntary reports of adverse events in people receiving either ENGERIX-B or HAVRIX that have been reported since market introduction of the vaccines include the following:

Body as a Whole: Anaphylaxis/anaphylactoid reactions and allergic reactions.^a

Hypersensitivity: Erythema multiforme including Stevens-Johnson syndrome,^b angioedema,^b arthritis,^b serum sickness–like syndrome days to weeks after vaccination including arthralgia/arthritis (usually transient), fever, urticaria, erythema multiforme, ecchymoses, and erythema nodosum.^b

Cardiovascular System: Tachycardia/palpitations.^b

Skin and Appendages: Erythema multiforme,^a hyperhidrosis,^a angioedema,^a eczema,^b herpes zoster,^b erythema nodosum,^b alopecia.^b

Gastrointestinal System: Jaundice,^a hepatitis,^a abnormal liver function tests,^b dyspepsia.^b

Hematologic/lymphatic: Thrombocytopenia.^b

Nervous System: Convulsions,^a paresis,^b encephalopathy,^a neuropathy,^{a+b} myelitis,^a Guillain-Barré syndrome,^{a+b} multiple sclerosis,^{a+b} Bell's palsy,^b transverse myelitis,^b optic neuritis.^b

Respiratory System: Dyspnea,^a bronchospasm including asthma-like symptoms.^b

Special Senses: Conjunctivitis,^b keratitis,^b visual disturbances,^b tinnitus,^b earache.^b

Other: Congenital abnormality.^a

^aFollowing HAVRIX.

^bFollowing ENGERIX-B.

^{a+b}Following either HAVRIX or ENGERIX-B.

DOSAGE AND ADMINISTRATION

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

For individuals with clotting factor disorders who are at risk of hemorrhage following intramuscular injection, the ACIP recommends that when any intramuscular vaccine is indicated for such patients, “. . . it 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 vaccination can be scheduled shortly after such therapy is administered. A fine needle (23 gauge or smaller) can be used for the vaccination and firm pressure applied to the site (without rubbing) for at least 2 minutes. The patient should be instructed concerning the risk of hematoma from the injection.”²⁸

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

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, TWINRIX 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.

Primary immunization for adults consists of 3 doses, given on a 0-, 1-, and 6-month schedule. Each 1-mL dose contains 720 EL.U. of inactivated hepatitis A virus and 20 mcg of hepatitis B surface antigen.

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

TWINRIX is supplied as a slightly turbid white suspension in vials and prefilled TIP-LOK[®] syringes containing a 1.0-mL single dose.

Single-Dose Vials

NDC 58160-850-01 (package of 1)

NDC 58160-850-11 (package of 10)

Single-Dose Prefilled Disposable TIP-LOK Syringes (packaged without needles)

NDC 58160-850-46 (package of 5)

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