IMMUNIZATION PROTOCOL FOR PHARMACISTS

COMBINED ADULT HEPATITIS A INACTIVATED AND HEPATITIS B RECOMBINANT VACCINE (Twinrix®)

Revisions as of 01/06:

- Updated Vaccine Schedule (Section IV). Minimum spacing between dose 2 and dose 3 is now 5 months instead of 8 weeks.
- Revised table B (Section V) on Integrating Twinrix with single antigen HepA and HepB vaccine.
- Recommendations for Use (Section III) updated to reflect high-risk settings along with some high-risk behavior.

I. ORDER:

1. Screen for contraindications.
2. Provide the current vaccine information statements (VIS) for both hepatitis A and B vaccines, answering questions.
3. Obtain a signed Vaccine Administration Record (VAR).
4. Give 1.0 ml intramuscularly into the deltoid muscle.
   a. Use formulation and dosage according to age and vaccine.
   b. Per the Immunization Program Medical Director, this vaccine may be given simultaneously with all other routine adult vaccines and travel vaccines according to the vaccination status of the recipient.[1]

NOTE: This vaccine has only been approved for pre-exposure prophylaxis at this time.

[1] While the concomitant use of this vaccine with other vaccines has not been studied, the vaccine may be used with other vaccines because it has the same contents as the Havrix® and Engerix® vaccines, which have been proven efficacious when given simultaneously with other routine vaccines.

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Pharmacist signature Date

Electronic copy of this protocol available at:
http://www.oregon.gov/dhs/ph/imm/provider/pharmpro.shtml
To request material in an alternate format (e.g., Braille), call (971) 673-0300.

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II. LICENSED TWINRIX® VACCINE

PRODUCT NAME	**Vaccine component(s)**	**Acceptable Age Range**	THIMEROSAL
Twinrix®[1,2]	Hepatitis A (Havrix®) Hepatitis B (Engerix-B®)	≥18 years	Trace (< 1mcg)

[1] Schedules using combinations of Twinrix® and single-antigen hepatitis A vaccines have not been studied. Guidelines for use of Twinrix® to complete a hepatitis A vaccine series begun with monovalent vaccine and for use of monovalent vaccine to complete a series begun with Twinrix® can be accessed in Section V. table B.

[2] Twinrix® is NOT approved for use in persons <18 years of age.

III. RECOMMENDATIONS FOR USE

Pre-exposure Prophylaxis

1. All unvaccinated adults at risk for hepatitis B virus (HBV) and hepatitis A virus (HAV) infections and adults seeking protection from these viruses (e.g., health and public safety workers) should be vaccinated.
2. In the following high risk settings all unvaccinated adults should receive vaccine
   - Sexually transmitted disease (STD) testing and treatment facilities,
   - Human immunodeficiency virus (HIV) testing and treatment facilities,
   - Facilities providing drug abuse treatment and prevention,
   - Correctional facilities,
   - College health services,
   - Chronic hemodialysis facilities and end-stage renal disease programs,
   - Institutions and nonresidential daycare facilities for developmentally disabled persons.
3. Hepatitis C-positive individuals
4. Alaska Natives and Pacific Islanders.
5. Individuals engaged in commercial sex work.
6. International travelers spending 6 months or more in an area with high rates of HBV infection and who will have close contact with the local population.

<u>Preparing for International Travel:</u>

If there is inadequate time to complete the 3-dose series, immunization should be initiated at least 4 weeks prior to expected exposure to HAV, which may allow up to 2 doses of Twinrix® to be administered. The manufacturer of Twinrix® reports that during clinical trials, 93.8% of participants seroconverted to hepatitis A following their first dose of Twinrix®; therefore, protection may be assumed 4 weeks after receipt of the first dose of vaccine, although the second and third doses of the series are needed for long-term protection.

IV. VACCINE SCHEDULE:

Schedule using Twinrix® only Route: IM into deltoid

DOSE	MINIMUM AGE[2,3]	DOSE VOLUME[1]	MINIMUM SPACING[2,3]	RECOMMENDED SPACING
1	≥ 18 years	1.0 ml		
2		1.0 ml	4 weeks after dose #1	4 weeks after dose #1
3		1.0 ml	≥ 5 months after dose #2 and ≥ 6 months after dose #1[4]	6-12 months after dose #2

[1] A 1.0 ml dose of Twinrix® provides 720 EL.U of inactivated hepatitis A virus and 20 mcg of recombinant hepatitis B surface antigen (HBsAg) protein. The amount of hepatitis A antigen (720 EL.U) in one adult dose of Twinrix® is the same as that contained in one pediatric dose of the monovalent hepatitis A vaccine, Havrix®.

[2] For retrospective checking, doses that violate the minimum spacing or age by 4 or fewer days do not need to be repeated. Doses administered 5 days or earlier than the minimum interval or age should be repeated as age-appropriate.

[3] When an invalid dose needs to be repeated, the repeat dose should be spaced after the invalid dose by a time equal to or greater than the minimum interval between doses,

[4] New ACIP reference on pg. 184 of 8th Edition "Pink Book" (second printing 1/05).

V. VACCINE INTERCHANGEABILITY

Although studies show that adults immunized with different formulations of the same monovalent vaccine respond similarly, ACIP recommends completion of any vaccination regimen with the same product whenever possible. However, if the originally used product is not available or known, vaccination with another monovalent product or with a combined vaccine is acceptable, provided that guidelines for dosage, age and spacing are respected. The recommended intervals between doses for the hepatitis A, hepatitis B, and Twinrix® vaccines differ from each other and must still be observed. Ages for the hepatitis A, hepatitis B, and Twinrix® vaccines differ from each other and must also be observed. Prior to switching an individual from Twinrix® to a single-antigen vaccine or vice-versa, please review the following tables:

V. Table A.
Minimum Spacing for single antigen Hepatitis A and Hepatitis B vaccines

	Two-Dose Series	**Three-Dose Series**	**Adolescent (1.0 ml) Recombivax®[1] Two-Dose Series**
Hepatitis A vaccine	≥6 months after dose #1		
Hepatitis B vaccine		≥ 4 weeks between the 1st and 2nd doses ≥ 8 weeks between the 2nd and 3rd doses; and ≥16 weeks between the 1st and 3rd doses	≥4 months after dose #1

[1]This two-dose series for 11-15 year olds should be completed by 16 years of age and is only approved for use with Recombivax® HB vaccine.

V. Table B Twinrix® schedule integrated with Single Antigen Hepatitis A (1.0 ml dose) vaccine

Dose 1	**Dose 2**	**Dose 3**
Twinrix®	Adult HA Vaccine[1]	Adult HA Vaccine[2]
Twinrix®	Twinrix®[1]	Adult HA Vaccine[2]
Adult HA Vaccine	Twinrix®[1]	Twinrix®[2]

[1] Separated by ≥ 4 weeks from 1st dose of Twinrix® or HA vaccine.
[2] Separated by ≥ 5 months from 2nd dose of Twinrix® or HA vaccine and ≥6 months from 1st dose of Twinrix® or HA vaccine.

V. Table C Twinrix® schedule integrated with Single Antigen Hepatitis B (1.0 ml dose) vaccine

Dose 1	**Dose 2**	**Dose 3**
Twinrix®	Adult HB Vaccine[3]	Adult HB Vaccine[4]
Twinrix®	Twinrix®[3]	Adult HB Vaccine[4]
Adult HB Vaccine	Twinrix®[3]	Twinrix®[4]
Adult HB Vaccine	Adult HB Vaccine[4]	Twinrix®[4]

[3]Separated by ≥ 4 weeks from 1st dose HB or Twinrix vaccine.
[4] Separated by ≥ 5 months from 2nd dose (Twinrix or HB vaccine) and ≥ 6 months from 1st dose of Twinrix or HB vaccine.

VI. CONTRAINDICATIONS	**VII. PRECAUTIONS**
A. Hypersensitivity to the adjuvants aluminum phosphate and aluminum hydroxide, preservative 2-phenoxyethanol, neomycin, yeast, or to any component of the vaccine contraindicates further use. B. Moderate or severe acute illness, with or without fever. C. The vaccine is also contraindicated for use in persons with a history of hypersensitivity to Twinrix® or to the monovalent hepatitis A or hepatitis B vaccines.	A. Pregnancy: The risk of vaccination should be weighed against the risk for hepatitis A in women who may be at high risk for exposure to hepatitis A virus. No animal-reproduction studies have been conducted with Twinrix® to date. B. Pregnancy Exposure Registry: Health-care providers are encouraged to register pregnant women who receive Twinrix® in the GlaxoSmithKline vaccination pregnancy registry by calling 1-800-366-8900. C. Immunocompromised: No special precautions need to be taken when vaccinating immunocompromised persons.

IX. SIDE EFFECTS AND ADVERSE REACTIONS:

Event	**Frequency/Incidence**
37-41% Pain at injection site	1%-10% of injections
8-11% Redness/swelling at injection site	1%- 10% of injections
3-22% Headache	< 1% of injections
11-14% Fatigue	< 1% of injections

Source: Prescribing information for *Twinrix*®: *Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine,* Manufactured by SmithKline Beecham Biologicals, Rixensart, Belgium. Date of issuance: Nov. 2001

- When compared to the monovalent hepatitis A and hepatitis B vaccines, the incidence and profile of side effects have been similar.
- No serious adverse events have been attributed definitively to the combined hepatitis A and B vaccine.
- Vaccination of a person who is immune because of prior infection does not increase the risk for adverse events.

X. OTHER CONSIDERATIONS

For someone with a history of fainting with injections, a 15-minute observational period is recommended post immunization

XI. ADVERSE EVENT REPORTING:

Adverse events following immunization must be reported to the Vaccine Adverse Events Reporting System (VAERS) at 1-800-822-7967. Forms and procedures can be found at the VAERS website: www.vaers.org. In addition, a copy of the completed VAERS form should be sent to the patient's primary provider, per ORS 855-041-0510.

XII. REFERENCES:

1. FDA Approval for a combined hepatitis A and B Vaccine; MMWR, Vol. 50, No. RR-37, 9/21/01. website:http://www.cdc.gov/ncidod/diseases/hepatitis/twinrix/index.htm
2. Hepatitis A. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, eds. 8th ed. Washington, DC: Public Health Foundation, 2005: 177-189. Available at**: http://www.cdc.gov/nip/publications/pink/hepa.pdf**.
3. Hepatitis B. In*: Epidemiology and Prevention of Vaccine-Preventable Diseases* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, eds. 8th ed. Washington, DC: Public Health Foundation, 2005: 191-211.
4. General Recommendations on Immunizations, MMWR Vol. 51, No. RR-2, 2/8/02.
5. Package insert - Twinrix® May, 2002

For more information or to clarify any part of the above order, consult with the vaccine recipient's primary health care provider, or contact the Oregon Health Services Immunization Program at (971) 673-0300.