OREGON STATE PUBLIC HEALTH DIVISION, DHS
IMMUNIZATION PROGRAM

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

Revisions as of 7/07:

- New Accelerated Twinrix® Vaccine Schedule (Section IV B – page 5) This recently FDA-approved accelerated schedule allows 3 doses to be given within 3 weeks, followed by a booster dose 12 months later.

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 to 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 only 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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Signature Health Officer or Medical Provider Date

II. LICENSED TWINRIX® VACCINE

Product Name	Vaccine component(s)	Acceptable Age Range	Thimerosal
Twinrix®[1]	Hepatitis A (Havrix®) Hepatitis B (Engerix-B®)	≥ 18 years[2]	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.

II. 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 who will be spending ≥ 6 months 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 regular 3-dose series, consider using the accelerated schedule (page 5). Either schedule should be initiated at least 4 weeks prior to expected exposure to HAV, which allows up to 3 doses of Twinrix® to be administered, depending on which schedule is used. 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 all the doses of a series are needed for long-term protection.

IV. A. REGULAR VACCINE SCHEDULE

Schedule using Twinrix® only Route: IM into deltoid

DOSE	MINIMUM AGE[2,3]	DOSE VOLUME[1]	MINIMUM SPACING[2,3]	RECOMMENDED SPACING[4]
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[5] and ≥ 6 months after dose #1	6–12 months after dose #1

[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] Due to the high Hepatitis A positivity rate after two doses of Twinrix® (98.8%), if a 3rd Twinrix® dose was administered > 8 weeks but < 5 months after dose two, this final dose of the series does not need to be repeated.

[4] Source: FDA Approval for a combined hepatitis A and B Vaccine. MMWR 2001; 50 (RR-37).

[5] Source: Hepatitis A. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, Wolfe S, eds. 8th ed. Washington, DC: Public Health Foundation, 2005: p184.

IV. B. ACCELERATED VACCINE SCHEDULE[1,2]

Schedule using Twinrix® only Route: IM into deltoid			
DOSE	**MINIMUM AGE**	**DOSE VOLUME**	**RECOMMENDED SPACING**
1	18 years	1.0 ml	
2		1.0 ml	≥7 days after dose #1
3		1.0 ml	21–30 days after dose #1
4		1.0 ml	≥12 months after dose #1

[1]This schedule provides a favorable option for those at imminent risk for hepatitis A and B, such as the last-minute traveler to a country where hepatitis A or B are endemic; prison inmates; military personnel; and first responders in disaster situations.

[2] FDA approved this accelerated dosing schedule 4/2/07 after studies showed that the immune response of those who completed this series was comparable to those who received complete vaccination with separately administered hepatitis A and hepatitis B vaccines.

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. The recommended intervals between doses for the hepatitis A, hepatitis B, and Twinrix® vaccines differ from each other and must still 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® HepB vaccine.

V. Table B. Twinrix® schedule integrated with Single-Antigen Hepatitis A (1.0ml 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 HepA vaccine.
[2] Separated by ≥ 5 months from 2nd dose of Twinrix® or HepA vaccine and ≥6 months from 1st dose of Twinrix® or HepA Vaccine.

V. Table C. Twinrix® schedule integrated with Single-Antigen Hepatitis B (1.0ml 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[3]	Twinrix®[4]

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

VI. CONTRAINDICATIONS

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.

VII. PRECAUTIONS

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.

VIII. 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. Nov. 2001

- When compared to the monovalent hepatitis A and hepatitis B vaccines, the incidence and profile of side effects with Twinrix® 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.

IX. OTHER CONSIDERATIONS

1. For someone with a history of fainting with injections, a 15-minute observational period is recommended post immunization.
2. Data from 11 clinical trials of 17-70 year olds indicated that 1 month after completion of the three dose Twinrix® series, seroconversion for antibodies against hepatitis A virus was 99.9%; after two doses the seroconversion rate was 98.8% and after one dose, 93.8%.
3. Data from a randomized comparative study of 496 healthy adults ≥18 years of age showed that individuals who completed the 4-dose series of Twinrix® on the accelerated dosing schedule had an immune response comparable to those who received complete vaccination with separately administered hepatitis A and hepatitis B vaccines.

X. ADVERSE EVENT REPORTING

Adverse events following immunization should be reported by public providers to the Oregon State Public Health Immunization Program, using a Vaccine Adverse Events Reporting System (VAERS) form, according to state guidelines. Private providers report all adverse events directly to VAERS, (800) 822-7967; the website address is www.vaers.org.

XI. REFERENCES

1. Trofa A, Glaxo-Smith Kline Biologicals. Rapid and sustained immune response against hepatitis A and B achieved with combined vaccine using an accelerated administration schedule. J Travel Medicine 2007; 14:9–15.
2. FDA approval for a combined hepatitis A and B vaccine. MMWR 2001; 50(37): 806–7.
3. 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, 2005:177–88.
4. 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.
5. General Recommendations on Immunizations, MMWR 2002; 51(RR-2).
6. Twinrix® Package insert, May, 2002.

For more information or to clarify any part of the above order, consult with your health officer or contact the State Public Health Immunization Program at (971) 673-0300.

To download this order visit our website at
http://oregon.gov/dhs/ph/imm/provider/stdgordr.shtml.
To request this material in an alternate format (e.g., braille), please call (971) 673-0300.