OREGON HEALTH AUTHORITY
IMMUNIZATION PROTOCOL FOR PHARMACISTS
COMBINED ADULT HEPATITIS A INACTIVATED AND
HEPATITIS B RECOMBINANT VACCINE (Twinrix®)

Revisions as of 12-21-2012:

- Removed footnote #3 of Section IV.A (p.4) Regular Vaccine Twinrix Schedule which stated “If a 3rd Twinrix® dose was administered >8 weeks but <5 months after dose two, this final dose does not need to be repeated.” No reference is available to support it.
- Updated references.

I. Order

1. Check the ALERT Immunization Information System to determine whether the patient needs this vaccine and any other vaccines.
2. Screen clients ≥18 years for contraindications.
3. Provide an Adolescent Well Visit Flyer to those 18 years of age.
4. Provide a current Vaccine Information Sheet (VIS) answering any questions.
5. Obtain a signed Vaccination Administration Record (VAR)
6. 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
7. Must be well shaken before administration to obtain a homogeneous, turbid, white suspension.2

NOTE: This vaccine is 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.

Immunizing Pharmacist Signature

For multiple signatures see: http://1.usa.gov/PharmacyImmunizationProtocols

Revised: 12-2012
Reviewed: 12-2013
Original: 01-2006
II. LICENSED Twinrix® VACCINE

<table>
<thead>
<tr>
<th>PRODUCT NAME</th>
<th>Vaccine component(s)</th>
<th>Acceptable Age Range</th>
<th>THIMEROSAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twinrix®¹,²</td>
<td>Hepatitis A (Havrix®) Hepatitis B (Engerix-B®)</td>
<td>≥18 years</td>
<td>Trace (&lt; 1mcg)</td>
</tr>
</tbody>
</table>

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. A. 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
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.

#### Preparing for International Travel:

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. A. VACCINE SCHEDULE:

**Schedule using Twinrix® only  Route: IM into deltoid**

<table>
<thead>
<tr>
<th>DOSE</th>
<th>MINIMUM AGE</th>
<th>DOSE VOLUME&lt;sup&gt;1&lt;/sup&gt;</th>
<th>MINIMUM SPACING&lt;sup&gt;2&lt;/sup&gt;</th>
<th>RECOMMENDED SPACING&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 18 years</td>
<td>1.0 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>1.0 ml</td>
<td>4 weeks after dose #1</td>
<td>4 weeks after dose #1</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>1.0 ml</td>
<td>≥ 5 months after dose #2&lt;sup&gt;4&lt;/sup&gt; and ≥ 6 months after dose #1</td>
<td>6-12 months after dose #2</td>
</tr>
</tbody>
</table>

<sup>1</sup> A 1.0ml 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®.

<sup>2</sup> 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.

<sup>3</sup> Source: FDA Approval for a combined hepatitis A and B Vaccine. MMWR 2001; 50 (RR-37).

## IV. B. ACCELERATED VACCINE SCHEDULE\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Schedule using Twinrix® only</th>
<th>Route: IM into deltoid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DOSE</strong></td>
<td><strong>MINIMUM AGE</strong></td>
</tr>
<tr>
<td>1</td>
<td>18 years</td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{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.

\textsuperscript{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 that of persons who received complete vaccination with separately administered hepatitis A and hepatitis B vaccines.

Reference: [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5640a5.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5640a5.htm)

## 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. TABLES Cont.

#### V. Table A. Minimum Spacing for Single-Antigen Hepatitis A and Hepatitis B vaccines

<table>
<thead>
<tr>
<th></th>
<th>Two-Dose Series</th>
<th>Three-Dose Series</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A vaccine</strong></td>
<td>≥6 months after dose #1</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis B vaccine</strong></td>
<td>≥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</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twinrix®</td>
<td>Adult HA Vaccine&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Adult HA Vaccine&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Twinrix®</td>
<td>Twinrix&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Adult HA Vaccine&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adult HA Vaccine</td>
<td>Twinrix&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Twinrix&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> Separated by ≥ 4 weeks from 1st dose of Twinrix® or HepA vaccine.
<sup>2</sup> 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

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twinrix®</td>
<td>Adult HB Vaccine&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Adult HB Vaccine&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Twinrix®</td>
<td>Twinrix&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Adult HB Vaccine&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adult HB Vaccine</td>
<td>Twinrix&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Twinrix&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adult HB Vaccine</td>
<td>Adult HB Vaccine&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Twinrix&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>3</sup> Separated by ≥ 4 weeks from 1st dose HepB or Twinrix® vaccine.
<sup>4</sup> 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 1-888-452-9622.

C. Latex: prefilled syringe tip caps and rubber plungers contain dry natural latex rubber. (per 2011 package insert)
VIII. SIDE EFFECTS AND ADVERSE REACTIONS

<table>
<thead>
<tr>
<th>Event</th>
<th>Frequency/Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>37-41% Pain at injection site</td>
<td>1%-10% of injections</td>
</tr>
<tr>
<td>8-11% Redness/swelling at injection site</td>
<td>1%-10% of injections</td>
</tr>
<tr>
<td>13-22% Headache</td>
<td>&lt; 1% of injections</td>
</tr>
<tr>
<td>11-14% Fatigue</td>
<td>&lt; 1% of injections</td>
</tr>
</tbody>
</table>

Source: Prescribing information for Twinrix®: Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine, Manufactured by GlaxoSmithKline. USA Date of issuance: Dec. 2009

- 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.

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 EVENTS 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.hhs.gov. In addition, a copy of the reporting form should be reported to the patient’s primary provider, per Oregon Revised Statute (ORS) 855-019-0280(4).

TABLE C. Events Reportable to VAERS

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Illness, disability, injury or condition covered</th>
<th>Time period until first symptom or the onset of significant reactions following vaccine administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccines containing Hepatitis B</td>
<td>Anaphylaxis or anaphylactic shock</td>
<td>4 hours</td>
</tr>
<tr>
<td></td>
<td>Any acute sequelae (including death)</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>


REFERENCES

1. CDC. Notice to Readers: FDA approval of an alternate dosing schedule for a combined Hepatitis A and B vaccine (Twinrix®). MMWR 2007; 56(40): 1057. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5640a5.htm
7. Package insert - Twinrix® March 2012 at
   www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110079.pdf

To request this material in an alternative format (e.g., Braille) or to clarify any part of the above order, contact the Oregon Health Authority Immunization Program at 971.673.0300 or 711 for TTY. For other questions, consult with the vaccine recipient’s primary health care provider or a consulting physician.

Electronic copy of this protocol available at:
   1.usa.gov/PharmacyImmunizationProtocols

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