

OREGON HEALTH AUTHORITY  
IMMUNIZATION PROGRAM  
HEPATITIS A VACCINES: **Havrix<sup>®</sup>1, Vaqta<sup>®</sup>2, Twinrix<sup>®</sup>3**

03-29-2016:

- Pre-exposure model standing order
- For post-exposure or travel prophylaxis see Hepatitis A Immune Globulin.
- New tables
- Addition of Twinrix<sup>®</sup>

**I. OREGON IMMUNIZATION MODEL STANDING ORDER:**

1. Check the ALERT Immunization Information System (IIS) to determine whether the patient needs this vaccine and any other vaccines.
2. Screen clients for contraindications.
3. Provide a current Vaccine Information Statement (VIS) and answer any questions.
4. Record all required data elements in the client's permanent health record.
5. Hepatitis A vaccine:
  - a) Give 0.5mL–1.0mL of Havrix<sup>®</sup> vaccine<sup>1</sup> intramuscularly (IM) to eligible clients. See Section IV. A. on page 8. **OR**
  - b) Give 0.5mL–1.0mL of Vaqta<sup>®</sup> vaccine<sup>2</sup> IM to eligible clients. See Section IV.B. on page 8. **OR**
  - c) Give 1.0mL of Twinrix<sup>®</sup> vaccine<sup>3</sup> IM to eligible clients. See Section IV. C.–D. on page 8.
6. This vaccine may be given with all ACIP–recommended child and adult vaccinations.
7. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.

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Signature	Health Officer or Medical Provider	Date
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Signature	Health Officer or Medical Provider	Date
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**This order expires July 31, 2017**

**II. LICENSED VACCINES\***

Product name	Vaccine component(s)	Acceptable age range	Latex	Thimerosal
<b>LICENSED MONOVALENT HEPATITIS A</b>				
Havrix <sup>®</sup> 1	Hepatitis A	≥ 1 years	Tip caps <b>may</b> contain natural rubber latex	None
Vaqta <sup>®</sup> 2	Hepatitis A	≥ 1 years	Vial stopper, syringe plunger stopper, and tip caps <b>contain</b> natural rubber latex	None
<b>LICENSED COMBINATION HEPATITIS A and B</b>				
Twinrix <sup>®</sup> 3 †§	Hepatitis A (Havrix <sup>®</sup> ) Hepatitis B (Engerix-B <sup>®</sup> )	≥ 18 years	Tip caps <b>may</b> contain natural rubber latex	Trace

\* Limited data suggest that vaccines from different manufacturers are interchangeable.

Completion of the hepatitis A vaccination series with vaccine from the same manufacturer is preferable, but if the initial vaccine product is unknown or unavailable, vaccination with either product is acceptable.<sup>4</sup>

† Schedules using a combination of Twinrix<sup>®</sup> and single-antigen hepatitis A vaccines have not been studied. Guidelines for use of Twinrix<sup>®</sup> to complete a hepatitis A vaccine series begun with monovalent vaccine and for use of monovalent vaccine to complete a series begun with Twinrix<sup>®</sup> have been provided by the Advisory Committee on Immunization Practices (ACIP). See Section IV. E. Vaccine Interchangeability table on page 10.<sup>4</sup>

§ Twinrix<sup>®</sup> is NOT approved for use in persons less than ≤17 years of age.<sup>3</sup>

### III. A. RECOMMENDATIONS FOR USE

#### A. Pre-exposure Prophylaxis—General

1. Hepatitis A vaccination is recommended by the ACIP for all children and adolescents aged  $\geq 1$  year of age.<sup>5</sup>
2. Vaccine is recommended for adults greater than 18 years of age at increased risk of infection, including:
  - Persons traveling to or working in countries that have a high or intermediate endemicity of infection<sup>5, 6, 7</sup>, including persons with travel related to international adoption.<sup>8</sup>
  - Household members and other close personal contacts (e.g., regular babysitters) of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity.<sup>5, 8</sup>
  - Men who have sex with men.<sup>5, 9</sup>
  - Injection drug users.<sup>5, 9</sup>
  - Persons working with non-human primates or with hepatitis A virus (HAV) in a research laboratory.<sup>5, 9</sup>
  - Persons who have chronic liver disease, Hepatitis B virus or Hepatitis C virus infections, or have received or are waiting for a liver transplant.<sup>5, 9</sup>
  - Persons who have clotting factor disorders (e.g., hemophilia).<sup>5, 9</sup>
  - All clients seen in STD clinics.<sup>5, 9</sup>
  - IG should be used for contacts  $< 12$  months or  $> 40$  years of age, are immunocompromised, or have chronic liver disease; and for contacts for whom vaccine is contraindicated.<sup>5, 6, 7</sup>
3. Any person wishing to obtain immunity.<sup>4</sup>

### III. B. RECOMMENDATIONS FOR USE Cont.

#### B. Pre-exposure Prophylaxis—Foreign Travel<sup>5, 6, 7, 9</sup>

1. All susceptible persons traveling to or working in countries that have high or intermediate hepatitis A endemicity should be vaccinated or receive IG before departure. Hepatitis A vaccination at the age-appropriate dose<sup>\*</sup> is preferred to IG.
2. For optimal protection, IG can be considered, in addition to vaccine, for older adults, immunocompromised persons, and persons with chronic liver disease or other chronic medical conditions who are traveling to an area within 2 weeks.
3. Travelers who elect not to receive vaccine, are <12 months of age, or are allergic to a vaccine component should receive a single dose of IG (0.02 ml/kg) which provides protection for up to 3 months. Travelers whose travel period will be >2 months should receive IG at 0.06 ml/kg; administration must be repeated if the travel period is >5 months.

<sup>\*</sup>Age 1–18 years: 0.5 ml; age ≥19 years: 1.0 ml.

### III. C. RECOMMENDATIONS FOR USE

#### 1. Pre-exposure Prophylaxis—Food Handlers<sup>5, 9</sup>

In general, persons working as food handlers in Oregon are not at increased risk for hepatitis A infection when compared to the general public. Therefore, it is not currently recommended that food handlers get immunized because of their occupation. Some food handlers however, do have other risks for hepatitis A (i.e. listed under III-A. General Pre-Exposure Prophylaxis-B), and should be immunized for their own protection.

### III. D. RECOMMENDATIONS FOR USE

#### 1. Post-Exposure

- Twinrix<sup>®</sup> is not recommended for post-exposure prophylaxis.<sup>9</sup>

### III. D. RECOMMENDATIONS FOR USE Cont.

2. Persons who have been exposed to hepatitis A within the past 14 days and who have never received hepatitis A vaccine should be administered a single dose of vaccine or IG (0.02 ml/kg) as soon as possible.\*<sup>5,</sup>

- For healthy persons **12 months–40 years of age, single-antigen hepatitis A vaccine at the age-appropriate dose is preferred to IG** because vaccine provides longer-lasting immunity and is easier to administer.<sup>6</sup>
- For persons >40 years of age, IG is preferred because hepatitis A is more severe, and the vaccine has not been shown to work following exposure for persons in this age group. If IG cannot be obtained, vaccine should be given.<sup>6, 7</sup>
- IG should be used for children aged <12 months, immunocompromised persons, persons with chronic liver disease, and persons for whom vaccine is contraindicated.<sup>5, 6, 7</sup>

\*Persons administered IG for whom hepatitis A vaccine is also recommended for other reasons should receive a dose of vaccine simultaneously with IG. The second dose of vaccine should be administered ≥6 months after the first dose to complete the series.

3. Prophylaxis should be administered according to the criteria above to unvaccinated persons in the following situations:<sup>5, 6, 7, 8, 9</sup>

- **Close personal contacts:** administer to all household, sexual, and illicit drug contacts of persons with serologically confirmed HAV infection.
- **Child care centers<sup>o</sup>:** administer to all previously unvaccinated staff and attendees of child care centers or homes if
  - a. One or more cases of hepatitis A are recognized in children or employees or
  - b. Cases are recognized in two or more households of center attendees. In centers that do not provide care to children who wear diapers, prophylaxis should be given only to classroom contacts of an index case.
  - c. When an outbreak occurs in a center, (i.e., HAV cases in 3 or more families), prophylaxis should also be given to unvaccinated household contacts of children in diapers who attend the center.

### III. D. RECOMMENDATIONS FOR USE Cont.

◇Persons who have never had hepatitis A and who have not been vaccinated, or have been vaccinated with only a single dose  $\geq 6$  months previously.

- **The confirmation of HAV infection** in the index patient by IgM anti-HAV testing is recommended prior to providing post-exposure prophylaxis to contacts. Contacts need not be serologically screened for immunity before giving IG or vaccine.
- Persons who have received 1 dose of hepatitis A vaccine at least 1 month prior to exposure should receive their 2nd dose of the series six months after dose #1.
- Should cost constraints require a choice between IG and vaccine for post-exposure prophylaxis, IG should be offered.
- **Food Handlers:** Hepatitis A is reportable, and the need for immunization of food-service co-workers or customers must be determined through investigation by local public health officials. Per OIP Medical Director.
- **Common-source exposure:**<sup>5</sup> Because common-source transmission to patrons at a food establishment is unlikely, prophylaxis of patrons usually is not recommended but may be considered if the following is true:
  - a. During the time when the food handler was likely to be infectious, the food handler both directly handled uncooked foods, or foods after cooking and had diarrhea or poor hygienic practices, and
  - b. Patrons can be identified and treated within 2 weeks of exposure.
    - In settings where **repeated exposures to HAV** may have occurred (e.g., institutional cafeterias), stronger consideration of vaccine may be warranted.
    - Other facilities where transmission has been known to occur are schools, hospitals, and other work settings where epidemiologic investigation indicates that transmission has occurred inside the facility.

**IV. VACCINE SCHEDULE**

<b>A. Havrix<sup>®1</sup> (GlaxoSmithKline)</b>					
AGE	DOSE (EL.U)	VOLUME	NUMBER OF DOSES	MINIMUM INTERVAL*	
1–18 years <sup>◇</sup>	720 EL.U	0.5ml	2	6 months	
≥19 years <sup>§</sup>	1440 EL.U	1.0ml	2 <sup>**</sup>	6 months <sup>‡</sup>	
<b>B. Vaqta<sup>®2</sup> (Merck)*</b>					
AGE	DOSE (U)	VOLUME	NUMBER OF DOSES	MINIMUM INTERVAL*	
1–18 years	25 U	0.5ml	2	6 months	
≥19 years <sup>§</sup>	50 U	1.0ml	2 <sup>**</sup>	6 months <sup>‡</sup>	
<b>C. Twinrix<sup>®3</sup> General Schedule (GlaxoSmithKline)</b>					
Minimum Age	DOSE (EL.U)		VOLUME	NUMBER OF DOSES	MINIMUM INTERVAL*
	A	B			
≥18 years	720 EL.U	20 mcg	1.0mL	1	
				2	4 weeks after dose #1
				3	6 to 12 months after dose 1
<b>D. Twinrix<sup>®3</sup> Accelerated Schedule (GlaxoSmithKline)</b>					
Minimum Age	DOSE (EL.U)		VOLUME	NUMBER OF DOSES	MINIMUM INTERVAL
	A	B			
≥18 years	720 EL.U	20 mcg	1.0mL	1	
				2	7 days after dose 1
				3	21–30 days after dose 1
				4 <sup>◇◇</sup>	≥12 months after dose 1

**IV. VACCINE SCHEDULE Cont.**

**A–D Footnotes:**

- \* For retrospective checking, doses that violate the minimum interval (to next dose) by 4 or fewer days do not need to be repeated.<sup>4</sup>
- ◊ For the 18 year old, check that the correct formulation is used for the appropriate dosage and schedule.<sup>1, 2, 3</sup>
- § The adult formulation of either vaccine must be used for persons 19 years of age and older; do not double the pediatric formulation to create an adult dose of vaccine.<sup>3</sup>
- ‡ The adult booster should be administered 6 to 12 months after the first dose.<sup>4</sup>
- \*\* For both vaccines, the booster dose given should be based on the person’s age at the time of the booster dose, not the age when the first dose was given.<sup>4</sup>
- ◊◊ A 4<sup>th</sup> dose may be forecasted for Twinrix<sup>®</sup> if the second dose is given less than 4 weeks after dose #1. This puts the series into the accelerated 4–dose schedule in ALERTIIS.

**E. 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.<sup>4</sup> The recommended intervals between doses for the hepatitis A, hepatitis B, and Twinrix<sup>®</sup> vaccines differ from each other and must still be observed. Prior to switching an individual from Twinrix<sup>®</sup> to a single-antigen vaccine or vice-versa, please review the following tables:

Table E. Single-Antigen Hepatitis a (1.0mL) and Twinrix <sup>®</sup> schedule integrated for persons ≥18 years of age		
Dose 1	Dose 2	Dose 3
Adult HA Vaccine	Twinrix <sup>◊</sup>	Twinrix <sup>§</sup>
Twinrix	Adult HA <sup>*◊</sup>	Adult HA <sup>*§</sup>
Twinrix	Twinrix <sup>◊</sup>	Adult HA <sup>*§</sup>

## E. VACCINE INTERCHANGEABILITY Cont.

Twinrix<sup>®</sup> is not recommended for post exposure prophylaxis.<sup>9</sup>

\* A 17 yr old should follow the same schedule using the pediatric HepA formulation (0.5 ml)

◇ Separated by  $\geq 4$  weeks from 1st dose of Twinrix<sup>®</sup> or HepA vaccine.

§ Separated by  $\geq 5$  months from 2nd dose of Twinrix<sup>®</sup> or HepA vaccine and  $\geq 6$  months from 1st dose of Twinrix<sup>®</sup> or HepA Vaccine

**Note:** At this time it has been demonstrated that healthy children and adolescents who have received two doses of VAQTA<sup>®</sup> can expect their hepatitis A antibody response to persist for at least five years. Healthy adults receiving two doses of VAQTA<sup>®</sup> were shown to have their hepatitis A antibody response last at least four years.

## V. CONTRAINDICATIONS

**Havrix<sup>®</sup>** and **Vaqta<sup>®</sup>**: A history of immediate and or severe allergic or hypersensitivity reactions (e.g., anaphylaxis) after a previous dose of any hepatitis A vaccine or with an anaphylactic reaction to neomycin.<sup>1, 2</sup>

**Twinrix<sup>®</sup>**: Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis A-containing or hepatitis B-containing vaccine, or to any component of TWINRIX, including yeast and neomycin.<sup>3</sup>

## VI. PRECAUTIONS

**Havrix<sup>®</sup>** and **Twinrix<sup>®</sup>**: Dry latex rubber in the tip cap may cause allergic reactions in latex-sensitive individuals.<sup>1, 3</sup>

**Vaqta<sup>®</sup>**: Dry natural rubber latex **is used** in the vial stopper, the syringe plunger stopper and tip cap.<sup>2</sup>

**Havrix<sup>®</sup>**, **Vaqta<sup>®</sup>** and **Twinrix<sup>®</sup>**: Vaccination should be deferred during a moderate or severe acute illness until symptoms have resolved.<sup>4</sup>

No special precautions need to be taken when vaccinating immunocompromised persons.<sup>9</sup>

Concomitant use with yellow fever and typhoid vaccines: The rate of seroconversion for hepatitis A antibodies following the first dose of VAQTA<sup>®</sup> or the concomitant administration of the first dose of VAQTA<sup>®</sup> with the yellow fever and typhoid vaccines is similar. The titers for hepatitis A following concomitant administration of VAQTA<sup>®</sup>, yellow fever and typhoid vaccines were adequate. Once the booster dose of VAQTA<sup>®</sup> was administered, the titers for hepatitis A between these two groups were comparable.<sup>2</sup>

**VII. SIDE EFFECTS AND ADVERSE EVENTS<sup>1</sup>**

Havrix <sup>®</sup>	Havrix <sup>®</sup>	Havrix <sup>®</sup>
Number followed for Safety	N =298	N=272
Age in Years	Adverse Reaction %	Adverse Reaction %
	15–24 months	15–24 months
Local Reaction, Injection site		
Pain	23.8	24.3
Redness	20.1	22.8
Swelling	8.7	9.6
Systemic Complaints		
Irritability	33.3	31.0
Fever ≥101.5	2.0	1.8
Alteration in appetite	18.3	19.9
Alteration in sleep	22.3	21.0
Table 1 page 5 <sup>1</sup>		

**VII. SIDE EFFECTS AND ADVERSE EVENTS<sup>2</sup>**

Vaqta <sup>®</sup>	Vaqta <sup>®</sup>	Vaqta <sup>®</sup>
Number followed for Safety	N =274	N=251
Age in Years	Adverse Reaction %	Adverse Reaction %
	12–23 months	12–23 months
Local Reaction, Injection site		
Pain	15.3	20.3
Redness	11.7	12.7
Swelling	9.5	7.6
Systemic Complaints		
Irritability	3.6	2.8
Fever ≥100.4	10.3	10
Table 1 and 2 page 4 and 5 <sup>2</sup>		

**VII. SIDE EFFECTS AND ADVERSE EVENTS<sup>3</sup>**

Twinrix <sup>®</sup>	Twinrix <sup>®</sup>	Twinrix <sup>®</sup>	Twinrix <sup>®</sup>
Number followed for Safety	N =385 Adverse Reaction %	N=382 Adverse Reaction %	N=374 Adverse Reaction %
Age in Years	18–70 years	18–70 years	18–70 years
Local Reaction, Injection site			
Pain	37	35	41
Redness	8	9	11
Swelling	4	4	6
Systemic Complaints			
Headache	22	15	13
Fatigue	14	13	11
Diarrhea	5	4	6
Nausea	4	3	2
Vomiting	1	1	0
Fever	4	3	2
Table 1 page 4 <sup>3</sup>			

1. Data from 11 clinical trials of 17-70 year olds indicated that 1 month after completion of the three dose Twinrix<sup>®</sup> 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%.<sup>3</sup>

2. 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<sup>®</sup> 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.<sup>3</sup>

**VIII. OTHER CONSIDERATIONS**

1. **Adverse Events:** epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case of anaphylactic or acute hypersensitivity reaction.<sup>4</sup>
2. **Immunocompromised:** Immunocompromised persons may have a diminished immune response to all Hepatitis A vaccines including individuals receiving immunosuppressant therapy.<sup>1, 2, 3</sup>
3. **Lactation:** It is not known whether Hepatitis A vaccines are excreted in human milk. Use with caution in nursing mothers.<sup>1, 2, 3</sup>
4. **Pregnancy:** Since vaccine is produced from inactivated Hepatitis A virus, the theoretical risk to the developing fetus is expected to be low when the vaccine is administered to a pregnant woman. 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.<sup>5</sup>

**IX. STORAGE AND HANDLING**

All clinics and pharmacies enrolled with the VFC program must **immediately** report any storage and handling deviations to their Oregon Immunization Program health educator. The health educator assignment map is located at: [http://bit.ly/HE\\_Map](http://bit.ly/HE_Map)

Vaccine	Temp	Storage Issues	Notes
Havrix <sup>® 1</sup>	Store at 2°–8°C	Do not use if vaccine has been frozen.	Report to health educator  Do not dilute to administer
Vaqta <sup>® 2</sup>	Store at 2°–8°C	Do not use if vaccine has been frozen.	Report to health educator
Twinrix <sup>® 3</sup>	Store at 2°–8°C	Do not use if vaccine has been frozen.	Report to health educator

**X.ADVERSE EVENTS REPORTING**

Public providers are to complete the Vaccine Adverse Events Reporting System (VAERS) report online at <https://vaers.hhs.gov/esub/step1>. Save a copy of the report number for your records, and send copies of the report and VAERS ID number to the Oregon Immunization Program Vaccine Safety Coordinator via confidential email at [ORVAERS.Reports@state.or.us](mailto:ORVAERS.Reports@state.or.us) or fax (971-673-0278). Private providers are to report events directly to VAERS and can read about options on how to do so at <http://vaers.hhs.gov/index>.

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 and 711 for TTY. For other questions, consult with the vaccine recipient's primary health care provider or a consulting physician.

Electronic copy of this standing order is available at:

<http://1.usa.gov/OregonStandingOrders>

## References

1. Havrix<sup>®</sup> (2013) package insert, available at:  
[www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224555.pdf](http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224555.pdf). Accessed 08 August 2015.
2. Vaqta<sup>®</sup> (2012) package insert, available at:  
[www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110049.pdf](http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110049.pdf) . Accessed 24 August 2015.
3. Twinrix<sup>®</sup> (2015) package insert, available at:  
[www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110079.pdf](http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110079.pdf) . Accessed 24 August 2015.
4. CDC. General Recommendations on Immunizations. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011; 60 (RR-2). Available at:  
[www.cdc.gov/mmwr/pdf/rr/rr6002.pdf](http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf) . Accessed 22 December 2015.
5. CDC. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 2006.; 55;1–30. Available at: <http://www.cdc.gov/mmwr/PDF/rr/rr5507.pdf> . Accessed 22 December 2015.
6. CDC. Update: Prevention of hepatitis A after exposure to hepatitis A virus an in international travelers. Updated recommendations of the Advisory Committee on Immunization practices (ACIP). MMWR, 2007;56:1080-83. Available at:  
[www.cdc.gov/mmwr/pdf/wk/mm5641.pdf](http://www.cdc.gov/mmwr/pdf/wk/mm5641.pdf) Accessed 4 November 2015.
7. Hepatitis A. In: Health Information for International Travel 2016. (“Yellow Book”). Kozarsky P, Magill A, Shlim D, eds. Atlanta: U.S. Department of Health and Human Services, Public Health Service, 2016. Available at:  
[wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/hepatitis-a](http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/hepatitis-a) . Accessed 24 August 2015.
8. CDC Updated recommendations form the ACIP on immunization practices for use of Hepatitis A vaccine in close contacts of newly arriving international adoptees. MMWR 2009; 58 (36) p. 1006-1007. Available at: [www.cdc.gov/mmwr/PDF/wk/mm5836.pdf](http://www.cdc.gov/mmwr/PDF/wk/mm5836.pdf) . Accessed 24 August 2015.
9. CDC. Hepatitis A FAQ for Health Professionals (2015). Available at:  
[www.cdc.gov/hepatitis/hav/havfaq.htm](http://www.cdc.gov/hepatitis/hav/havfaq.htm) . Accessed 24 August 2015.