

**OREGON HEALTH AUTHORITY
IMMUNIZATION PROGRAM**

**HUMAN PAPILOMAVIRUS (HPV) VACCINE
Quadrivalent and Bivalent**

Revisions on 12/2011 are based on new 10/2011 Advisory Committee on Immunization Practices (ACIP) Recommendations.

- Routine recommendation for HPV4 (3- dose series) for males ages 11–12 years.
- HPV series can be started in males as early as 9 years of age.
- Males 13–21 years not vaccinated should be given catch-up HPV4.
- Males 22–26 years may be vaccinated, but HPV4 is not recommended for routine use in this age group.

I. ORDER:

1. Screen for contraindications.
2. Provide the current Vaccine Information Statement (VIS), answering any questions.
3. Obtain a signed Vaccine Administration Record (VAR).
 - a. Give HPV vaccine (0.5 ml) intramuscularly (deltoid preferred) as appropriate for the age and sex of the patient.
 - b. Simultaneous vaccination may be given with all routine adolescent or adult vaccines.

Signature Health Officer or Medical Provider

Date

December 2011

II. LICENSED HUMAN PAPILLOMAVIRUS (HPV) VACCINE

Product Name	Vaccine components	Acceptable Sex and Age Range	Thimerosal
Gardasil® ¹ (HPV4)	Protein of HPV types 6,11, 16, and 18	Females 9–26 years, Males 9–26 years ²	None
Cervarix® ³ (HPV2)	Protein of HPV types 16 and 18	Females only, 9–26 years ⁴	None

¹ Designed to prevent HPV 6 & 11 type venereal warts and HPV 16 and 18 related cervical cancer, cervical dysplasias, and vulvar or vaginal dysplasias.

² ACIP recommends routine HPV4 for all males 9–21 years and for some males 22–26 years of age. See section III-4 for recommendations for special populations.

³ Designed to prevent HPV 16 and 18 related cervical cancer, cervical intraepithelial neoplasia grade 2 or worse and adenocarcinoma *in situ* and cervical intraepithelial neoplasia grade1.

⁴ Although the package insert indicates a 10–25 years age range, ACIP’s blended schedule (p 3) indicates that Cervarix® may be given to females 9–26 years of age..

III. RECOMMENDATIONS FOR USE:

1. Routine vaccination of females and males 11 – 12 years of age with 3 doses of HPV vaccine. The vaccine series can be started beginning at age 9 years.^{1, 2}
2. HPV vaccination is also routinely recommended for females 13–26 years of age not previously vaccinated or who have not completed the full HPV series.
 - Vaccinate with either the HPV2 or HPV4 for prevention of cervical cancers and pre-cancerous lesions.
 - Vaccinate with the HPV4 vaccine for prevention of cervical cancers, pre-cancerous lesions, and genital warts.³
3. Males aged 13–21 years who have not been vaccinated should be given catch-up HPV4.⁴
4. Immunosuppressed males and MSM 22–26 years of age should be vaccinated.^{4, 5}

¹ This vaccine is not recommended for use in pregnancy.

² Females and males who are immunocompromised either from disease or medication can receive HPV4 vaccine. However, the immune response and vaccine effectiveness might be less than in those who are immunocompetent.

³ HPV4 has also been demonstrated to protect against vulvar and vaginal cancers and pre-cancers.

⁴ HPV4 has also been demonstrated to protect against anal cancers and anal intraepithelial neoplasias. Gardasil® package insert at:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>

⁵ MMWR 2011 available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6050a3.htm>

IV. RECOMMENDED BLENDED VACCINE SCHEDULE FOR Gardasil® (HPV4)^{1, 2} and Cervarix® (HPV2)^{2, 3}

Dose and Route: 0.5 ml IM				
DOSE	RECOMMENDED AGE	MINIMUM AGE	RECOMMENDED SPACING	MINIMUM SPACING⁵
1	11–12 years ⁴	9 years		
2			1–2 months after 1 st dose	4 weeks after 1 st dose
3			6 months after 1 st dose	12 weeks after 2 nd dose
				24 weeks after 1 st dose ⁶

¹ Approved for use in males and females 9–26 years of age.
² Ideally, vaccine should be administered before potential exposure to HPV through sexual contact.
³ Approved for use in females 9–26 years of age.
⁴ While the ACIP-recommended age for vaccination is 11–12 years, in order to maximize the likelihood that females and males will complete the 3-dose HPV series, the Oregon Health Authority Immunization Program’s Medical Director and Immunization Policy Advisory Team have recommended that providers take advantage of any opportunity to vaccinate females and males as young as 9 years of age.
⁵ Minimum spacing may be used when a person is behind schedule and needs to be brought up-to-date as quickly as possible or when travel is imminent. Although the effectiveness of accelerated schedules has not been evaluated in clinical trials, the Advisory Committee on Immunization Practices (ACIP) believes that the immune response induced with accelerated schedules will be adequate.
⁶ The 3rd dose does not need to be repeated if, retrospectively, it was given at least 16 weeks after the 1st dose. (per Immunization Program medical director)
 Note: If the vaccine schedule is interrupted, the vaccine series does not need to be restarted.

V. CONTRAINDICATIONS

- A. For persons with a history of immediate hypersensitivity to any vaccine component.
- B. For GARDASIL®; a history of immediate hypersensitivity to yeast.
- C. For CERVARIX®; Do not use prefilled syringes for individuals who have had anaphylactic reactions to latex.

VI. PRECAUTIONS

- A. HPV vaccine can be administered to females with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infections, with or without fever).
- B. Vaccination of people with moderate or severe acute illnesses should be deferred until after the illness improves.
- C. Syncope after vaccination; Recommendation to observe patients for 15 minutes after receipt of HPV vaccine).

VII. A. SIDE EFFECTS AND ADVERSE REACTIONS WITH GARDASIL®

Table 1

Adverse Reactions in Females 9–26 yrs			
	Gardasil® (N = 5088)	AAHS Control¹ (N = 3470)	Saline Placebo (N = 320)
Injection Site (1-5 days post-vaccination)			
Pain	83.9%	75.4%	48.6%
Swelling	25.4%	15.8%	7.3%
Erythema	24.6%	18.4%	12.1%
Pruritus	3.1%	2.8%	0.6%
Systemic 1-15 days post-vaccination)		Placebo (N=3790)	
Fever	13.0%	11.2%	
Nausea	6.7%	6.5%	
1. Reference: Gardasil® package insert (pp.4 &6), available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf			

VII. A. SIDE EFFECTS AND ADVERSE REACTIONS WITH GARDASIL®

Table 2

Adverse Reactions in Males 9–26 yrs			
	Gardasil® (N = 3092)	AAHS Control¹ (N = 3470)	Saline Placebo (N = 320)
Injection Site 1–5 days post-vaccination			
Pain	61.4%	50.8%	41.6%
Erythema	16.7%	14.1%	14.5%
Swelling	13.9%	9.6%	8.2%
Systemic 1–15 days post-vaccination		Placebo (N=2303) %	
Headache	12.3%	11.2%	
Fever	8.2%	6.5%	
1. Reference: Gardasil® package insert (pgs 5 &7)available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf			

VII. B. SIDE EFFECTS AND ADVERSE REACTIONS WITH CERVARIX®

Within 7 days of vaccination^a

Table 3

Adverse Reactions in Females	CERVARIX (9–25 yrs)	HAV 720^b (15–25 yrs)	HAV 360^c (10–14 yrs)	Al(OH)₃ Control^d (15–25 yrs)
Local Adverse Reaction	N=6,669	N=3,079	N=1,027	N=549
Pain	91.9%	78.0%	64.2%	87.2%
Redness	48.4%	27.6%	25.2%	24.4%
Swelling	44.1%	19.8%	17.0%	21.3%
General Adverse Event	N=6,670	N=3,079	N=1,027	N=549
Fatigue	54.6%	53.7%	42.3%	53.6%
Headache	53.4%	51.3%	45.2%	61.4%
GI ^e	27.9%	27.3%	24.6%	32.8%
Fever (≥99.5°F)	12.9%	10.9%	16.0%	13.5%
Rash	9.5%	8.4%	6.7%	10.0%
	N=6,119	N=3,079	N=1,027	
Myalgia ^f	48.8%	44.9%	33.1%	
Arthralgia ^f	20.7%	17.9%	19.9%	
Urticaria ^f	7.2%	7.9%	5.4%	

a. Total vaccinated cohort included subjects with at least one documented dose (N).

b. HAV 720 = Hepatitis A Vaccine control group [720 EL.U. of antigen and 500 mcg Al(OH)₃]

c. HAV 360 = Hepatitis A Vaccine control group [360 EL.U. of antigen and 250 mcg of Al(OH)₃]

d. Al(OH)₃ Control = control contains 500 mcg Al(OH)₃

e. GI = Gastrointestinal symptoms, including nausea, vomiting, diarrhea, or abdominal pain

f. Adverse events solicited in a subset of subjects.

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf> p5

VIII. OTHER CONSIDERATIONS

- A. Pregnancy: HPV vaccines are not recommended for use in pregnancy. Data on vaccination during pregnancy are limited. If a vaccine dose has been administered during pregnancy no intervention is needed; but any exposure to Gardasil® vaccine during pregnancy should be reported to Merck's vaccine pregnancy registry at 800-986-8999; **OR** CERVARIX® Pregnancy Registry at 888-452-9622.
- B. Abnormal Pap test: This vaccine can be given to females who have an equivocal or abnormal Pap test, a positive Hybrid Capture II® high-risk test, or genital warts. However, vaccine recipients should be advised that data from clinical trials do not indicate that the vaccine will have any therapeutic effect on existing Pap test abnormalities, HPV infection or genital warts. Vaccination of these females would provide protection against infection with vaccine HPV types not already acquired.
- C. Nursing mothers may receive Gardasil® HPV vaccine per ACIP. Use caution with CERVARIX® per the package insert.
- D. Persons who are immunocompromised, either from disease or medication, may receive HPV vaccine. However, the immune response to vaccination and vaccine effectiveness might be less than in immunocompetent persons.
- E. Men who have sex with men (MSM) are 17 times more likely to develop anal cancer than men who only have sex with women. Men with HIV are more likely to get severe hard to treat cases of genital warts.
<http://www.cdc.gov/std/hpv/stdfact-hpv-and-men.htm>
- F. Preventing syncope after vaccination: Through January 2007, the second most common report to VAERS following receipt of HPV vaccine was syncope (CDC, unpublished data). Vaccine administrators should consider observing patients for 15 minutes after they receive HPV vaccine.
- G. Syncope, sometimes associated with tonic-clonic movements has been reported with CERVARIX®. This is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position.

IX. ADVERSE EVENT REPORTING

Adverse events following immunization should be reported by public providers to the Oregon Health Authority Immunization Program by FAX (971-673-0278) or mail according to state guidelines. Public provider reporting forms are available at: <http://bit.ly/PublicProvidersVAERSform>. Private providers report adverse events directly to VAERS at www.vaers.hhs.gov.

X. REFERENCES

1. CDC. Recommendations on the use of quadrivalent human papillomavirus vaccine in males (ACIP). MMWR 2011; 60:1705-8. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6050a3.htm>
2. ACIP VFC Resolution No. 010/11-1 for HPV Vaccines, available at <http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/10-11-1-hpv.pdf>
3. CDC. FDA licensure of quadrivalent human papillomavirus vaccine (HPV4, Gardasil) for use in males and guidance from the advisory committee on immunization practices (ACIP). MMWR 2010; 59 (20); available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a5.htm?s_cid=mm5920a5_e
4. CDC. Quadrivalent human papillomavirus vaccine. ACIP Recommendations for Use. MMWR 2007; 56. Available at <http://www.cdc.gov/mmwr/pdf/rr/rr5602.pdf>
5. Human Papillomavirus. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, eds. 1^{2th} ed. Washington, DC: Public Health Foundation, 2011 139–50. Available at <http://www.cdc.gov/vaccines/pubs/pinkbook/index.html>
6. Merck & CO. Inc. Gardasil® package insert. Available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>
7. GlaxoSmithKline. CERVARIX® package insert. Available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf>

For more information or to clarify any part of the above order, consult with your health officer or call the Oregon Health Authority Immunization Program at 971-673-0300.

For a copy of this order visit our website at
<http://1.usa.gov/OregonStandingOrders>

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