# HPV Vaccine Information for Clinicians

**CDC recommends HPV vaccination for girls and boys at ages 11 or 12 years to protect against cancers caused by HPV infections. CDC encourages clinicians to recommend HPV vaccination the same way and same day they recommend other routinely recommended vaccines for adolescents.**

## Background

Human papillomaviruses (HPV) are a very common family of viruses that infect epithelial tissue. More than 120 HPV types have been identified. Most HPV types infect cutaneous epithelial cells and cause common warts, such as those that occur on the hands and feet. Approximately 40 HPV types can infect mucosal epithelial cells, such as those on the genitals, mouth, and throat. Although most HPV infections are asymptomatic and resolve spontaneously or become undetectable, some HPV infections can persist and lead to cancer.

Persistent infections with high-risk (oncogenic) HPV types can cause cervical, vaginal and vulvar cancers in women; penile cancers in men; and oropharyngeal and anal cancers in both men and women. The most common high-risk types are HPV 16 and 18.

Infection with low-risk (non-oncogenic) HPV types can cause genital warts and rarely laryngeal papillomas. These types can also cause benign or low-grade cervical cell abnormalities. The most common low-risk types are HPV 6 and 11.

About 79 million Americans are infected with genital HPV. Approximately 14 million people become newly infected each year, mostly teens and young adults. Almost every person will acquire an HPV infection at some time in their life.

Every year in the United States, an estimated 19,200 women and 11,600 men are diagnosed with a cancer caused by HPV infection.

Of women diagnosed with an HPV cancer, cervical cancer is the most common with almost 12,000 women diagnosed annually in the United States; subsequently about 4,400 women die every year from cervical cancer in the country.

Of the men in the United States diagnosed with an HPV cancer, oropharyngeal cancer is the most common. Around 9,100 U.S. men each year are diagnosed with oropharyngeal cancer caused by HPV infection. There is no screening test for oropharyngeal cancers, making prevention of infection a priority.

## HPV Vaccines

Three HPV vaccines have been licensed by the U.S. Food and Drug Administration (FDA) since 2006. HPV vaccine is recommended for routine vaccination of adolescents (including girls and boys) at age 11 or 12 years, and can be started at age 9 years.

| | Bivalent/2vHPV (Cervarix) | Quadrivalent/4vHPV (Gardasil) | 9-valent/9vHPV (Gardasil 9) |
|---|---|---|---|
| **Manufacturer** | GlaxoSmithKline | Merck | Merck |
| **Year Licensed** | October 2009 - females | June 2006 - females; October 2009 - males | December 2014 - males and females |
| **HPV types in vaccine** | 16 and 18 | 6, 11, 16, and 18 | 6, 11, 16, 18, 31, 33, 45, 52, and 58 |
| **Adjuvant in vaccine** | AS04: 500 µg aluminum hydroxide<br>50 µg 3-*O*-desacyl-4′-monophosphoryl lipid A | AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate | AAHS: 500 µg amorphous aluminum hydroxyphosphate sulfate |
| **Recommended for…** | • Females ages 11-12 (can start at age 9 years)<br>• Females ages 13 through 26 who were not adequately vaccinated previously | • Females and males ages 11-12 (can start at age 9 years)<br>• Females ages 13 through 26 and males ages 13 through 21 who were not adequately vaccinated previously<br>• Males ages 22 through 26 with certain immunocompromising conditions; gay, bisexual, and other men who have sex with men (MSM); and transgender persons who were not adequately vaccinated previously | • Females and males ages 11-12 (can start at age 9 years)<br>• Females ages 13 through 26 and males ages 13 through 21 who were not adequately vaccinated previously<br>• Males ages 22 through 26 with certain immunocompromising conditions; gay, bisexual, and other men who have sex with men (MSM); and transgender persons who were not adequately vaccinated previously |
| **Contraindicated for…** | People with anaphylaxis caused by latex | People with immediate hypersensitivity to yeast | People with immediate hypersensitivity to yeast |

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Bivalent HPV vaccine protects against two types of HPV, quadrivalent HPV vaccine protects against four types of HPV, and 9-valent HPV vaccine protects against nine types of HPV. Bivalent, quadrivalent, and 9-valent HPV vaccine all protect against HPV 16 and 18, the HPV types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States. Quadrivalent and 9-valent HPV vaccine also protect against HPV 6 and 11, the HPV types that cause anogenital warts. In addition, 9-valent HPV vaccine targets five additional cancer-causing types, which account for another 15% of cervical cancers (12).

The additional five types in 9-valent HPV vaccine account for a higher proportion of HPV-associated cancers in women compared with men, and also cause cervical precancers in women. Therefore, the additional protection from 9-valent HPV vaccine will mostly benefit women.

After the end of 2016, only 9-valent HPV vaccine will be available in the United States.

## HPV Vaccine Recommendations

HPV vaccine is routinely recommended for adolescents at age 11 or 12 years. Vaccination is also recommended for females ages 13 through 26 years and males ages 13 through 21 years who were not adequately vaccinated when they were younger. Vaccination is also recommended for gay, bisexual, and other men who have sex with men, transgender people, and persons with certain immunocompromising conditions ages 22 through 26 years who were not adequately vaccinated when they were younger.

Ideally, adolescents should be vaccinated before they are exposed to HPV. However, people who have already been infected with one or more HPV types can still get protection from other HPV types in the vaccine.

### HPV vaccines *can* safely be given to…

- Patients with minor acute illnesses, such as diarrhea or mild upper respiratory tract infections, with or without fever.
- Women who have had an unclear or abnormal Pap test, a positive HPV test, or genital warts. However, these patients should be advised that the vaccine may not have any therapeutic effect on existing Pap test abnormalities, HPV infection, or genital warts.
- Patients with immunocompromising conditions, including certain diseases or medications. However, the immune response to vaccination and effectiveness of the vaccine might be less than in people with a normally functioning immune system.
- Women who are breastfeeding.

### HPV vaccines should *not* be given to…

- Patients with a history of allergies to any vaccine component. Quadrivalent vaccine (4vHPV) and nine-valent vaccine (9vHPV) are not recommended for people with immediate hypersensitivity to yeast. Bivalent vaccine (2vHPV) is not recommended for people with anaphylaxis caused by latex.
- Patients with moderate or severe acute illnesses. In these cases, patients should wait until the illness improves before getting vaccinated.
- Pregnant women. However, HPV vaccines have not been shown to cause any adverse pregnancy outcomes or adverse events for the mother or her developing fetus.
  - If a woman is found to be pregnant after starting the HPV vaccine series, second and/or third doses should be delayed, and given after she is no longer pregnant.
  - Pregnancy testing is not needed before vaccination. If a pregnant woman does receive HPV vaccine, no intervention is needed.
  - Exposure to 9vHPV vaccine during pregnancy can be reported to the manufacturer. Pregnancy registries for 4vHPV and 2vHPV were closed after >6 years, with FDA concurrence.

## HPV Vaccine Safety

HPV vaccines are very safe. Scientific research shows the benefits of HPV vaccination far outweigh the potential risks. Like all medical interventions, vaccines can have some side effects. Nearly 90 million doses of HPV vaccines have been distributed in the United States since the first HPV vaccine was introduced in 2006. The most common side effects associated with HPV vaccines are mild, and include pain, redness, or swelling in the arm where the shot was given.

All vaccines used in the United States, including HPV vaccines, are required to go through years of extensive safety testing before they are licensed by the U.S. Food and Drug Administration (FDA). During clinical trials conducted before they were licensed:

- 9-valent HPV vaccine was studied in more than 15,000 males and females
- Quadrivalent HPV vaccine was studied in more than 29,000 males and females
- Bivalent HPV vaccine was studied in more than 30,000 females
- Each HPV vaccine was found to be safe and effective.

Syncope (fainting) can occur after any medical procedure, including vaccination. Recent data suggest that syncope after any vaccination is more common in adolescents. Adolescents and adults should be seated or lying down during vaccination, and remain that way for 15 minutes after vaccination, under clinician observation. This is to prevent any injuries that could occur from a fall during a syncopal event.

Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Additional information about VAERS is available by telephone (1-800-822-7967) or online (https://vaers.hhs.gov).

## HPV Vaccine Effectiveness

HPV vaccines work extremely well. HPV vaccine was first recommended in 2006 in the United States, and by 2010, quadrivalent type HPV infections in teen girls decreased by 56%, and decreases in prevalence were also observed in women in their early 20s. Research has also shown that fewer U.S. teens are getting genital warts since HPV vaccines have been in use. Also, decreases in vaccine-type prevalence, genital warts, and cervical dysplasia have been observed in other countries with HPV vaccination programs.

There are no data to suggest HPV vaccines will treat existing diseases or conditions caused by HPV. However, people who already have HPV-associated diseases or conditions can still get protection from other HPV types covered by the vaccines.

Cervical cancer screening is recommended for women beginning at age 21 years and continuing through age 65 years for both vaccinated and unvaccinated women. Women who have received any HPV vaccine should still be screened for cervical cancer beginning at age 21 years, in accordance with currently published cervical cancer screening guidelines. There are no screening recommendations for other cancers caused by HPV.

## Duration of Vaccine Protection

Studies suggest that HPV vaccines offer long-lasting protection against HPV infection and therefore disease caused by HPV infection. Studies of the bivalent and quadrivalent vaccines have followed vaccinated individuals for around ten years, and so far have found no evidence of protection decreasing over time. Duration of protection provided by HPV vaccination will continue to be studied.

## HPV Vaccine Dosing Schedules

- If the first dose of any HPV vaccine is given before the 15th birthday, vaccination should be completed according to a 2-dose schedule. In a 2-dose series, the second dose is recommended 6–12 months after the first dose (0, 6–12 month schedule).
- If the first dose of any HPV vaccine is given on or after the 15th birthday, vaccination should be completed according to a 3-dose schedule. In a 3-dose series, the second dose is recommended 1–2 months after the first dose, and the third dose is recommended 6 months after the first dose (0, 1–2, 6 month schedule).
- In a 2-dose schedule of HPV vaccine, the minimum interval is 5 months between the first and second dose. If the second dose is administered at a shorter interval, a third dose should be administered a minimum of 12 weeks after the second dose and a minimum of 5 months after the first dose.
- In a 3-dose schedule of HPV vaccine, the minimum intervals are 4 weeks between the first and second dose, 12 weeks between the second and third dose, and 5 months between the first and third dose. If a vaccine dose is administered at a shorter interval, it should be re-administered after another minimum interval has been met since the most recent dose.

Although minimum intervals are stated in the dosing schedule, there is no maximum interval. There is no reason to restart the vaccine series if the HPV vaccine schedule is interrupted; patients who have exceeded the minimum interval for the next dose by months or even years, may be given the next dose needed. 9-valent HPV vaccine may be used to continue or complete a vaccination series started with quadrivalent or bivalent HPV vaccines.

There is no ACIP recommendation regarding additional 9-valent HPV vaccine doses for persons who have been adequately vaccinated with bivalent or quadrivalent HPV vaccine.

HPV vaccine can safely be administered at the same visit as other vaccines recommended for adolescents at ages 11 or 12 years, such as tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine, quadrivalent meningococcal conjugate (MenACWY) vaccine, and influenza vaccine. Administering all indicated vaccines at a single visit at ages 11 or 12 years increases the likelihood that patients receive their vaccinations on schedule.

As mentioned previously, patients should be observed for 15 minutes after receiving any shot, including HPV vaccine.

## Paying for HPV Vaccine

As with all vaccines recommended by the Advisory Committee on Immunization Practices (ACIP), HPV vaccines are covered by insurance. For patients that need assistance paying for HPV vaccine, the Vaccines for Children (VFC) program may be able to help. VFC provides vaccines for children ages 18 years and younger who are uninsured, Medicaid-eligible, or American Indian/Alaska Native. Learn more about the VFC program at www.cdc.gov/Features/VFCprogram.

## Related Resources


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