

Human Papillomavirus (HPV) Vaccine

The Immunization Practices Advisory Council (IPAC), a collaborative of the New Mexico Department of Health and the New Mexico Immunization Coalition, urge all medical practices and health professionals to routinely administer a series of 3 injections of human papillomavirus vaccine to males and females ages 11 or 12 years. Females may be given HPV quadrivalent vaccine, Gardasil[®], the nine valent vaccine, Gardasil 9, (both from Merck), or HPV Bivalent Vaccine, Cervarix[®] (GlaxoSmithKline), whereas males should be given quadrivalent or nine valent vaccine (Gardasil[®] and Gardasil 9 respectively). This recommendation is based on observations that HPV vaccine is most beneficial when provided before sexual activity begins. Most sexually active people become infected with genital tract HPV shortly after sexual initiation. The vaccine is not effective against HPV types already acquired, but will protect against any of the HPV types to which the recipient has not been exposed.

At the discretion of the clinician, the series may be started in children as young as 9 years of age. The HPV vaccine is also indicated for adolescents and adults between the ages of 13 and 26 years of age who have not received the vaccine.

HPV and Cancer

HPV infection is the most common sexually transmitted infection in the United States and causes a majority of atypical squamous cells of undetermined significance (ASCUS), more than 90% of all cervical intraepithelial neoplasia (CIN 1,2,3), and virtually all invasive cervical cancers. HPV 16 and 18 are responsible for up to 70% of CIN and cervical cancer and also 25 – 70% of vaginal and vulvar intraepithelial neoplasia (VaIN and VIN, respectively) as well as substantial causes of anal and penile carcinoma in males.

HPV Vaccine

HPV vaccine prevents cancer-causing infection. While originally recommended for only females, the ACIP/CDC began to recommend HPV vaccination for adolescent males as well which may lower the risk of transmission of oncogenic and wart-producing HPV types to sexual partners and prevent HPV-related cancers in both males and females. It is also one of the three routine adolescent vaccines recommended by the ACIP/CDC and endorsed by AAP and AAFP. The CDC (2013) recommends that providers immunize adolescents during episodic as well as preventive visits in order to avoid missed opportunities. In New Mexico, adolescents seeking confidential services may also consent for HPV vaccines as part of treatment and prevention of sexually transmitted infections. Gardasil[®] is a recombinant product of highly purified virus-like particles (VLPs) of HPV capsid proteins produced in yeast. Cervarix[®] contains similar VLPs produced in insect cells. Neither vaccine contains any live HPV viral particles and cannot transmit HPV infection.

Gardasil 9

In December 2014, the FDA approved Gardasil 9 vaccine that protects against an additional 20% of cervical cancers related to HPV: 31, 33, 45, 52, and 58 as well as 6, 11, 16, and 18. Gardasil 9 is approved for males and females starting at age 9. A series of 3 injections is recommended to be administered similarly to the current Gardasil vaccine. In February 2015, the ACIP approved use of this vaccine.

HPV Types covered by the various vaccines is summarized in the table below

HPV Types	Protection provided	Gardasil [®] 9 (nonavalent)	Gardasil [®] (quadrivalent)	Cervarix [®] (bivalent)
16 and 18	Cause 70% of cervical, oral and urogenital cancers	✓	✓	✓
6 and 11	Cause 90% of genital warts	✓	✓	
31, 33, 45, 52, 58	Protects against an additional 20% of cervical cancers	✓		

Gardasil[®] and Cervarix[®] may provide additional cross protective coverage for some other oncogenic types, particularly 31 and 45, but neither vaccine is specifically approved by the FDA for this indication; see each package insert for further details.

What is the administration schedule?

Gardasil[®] and Cervarix[®] are provided as either single dose vials or prefilled syringes; neither are provided in multi-dose vials. Both vaccines must be stored in refrigeration at temperatures of 2-8° C (36-45° F) and must be administered as soon as possible after removed from refrigeration. HPV vaccines are administered as a series of 0.5mL intra muscular injections using the following schedule.

Vaccine	First dose	Second dose	Third dose
Cervarix® (Bivalent)	Females 11-26 (min. age 9)	Minimum interval 1-2 months after the first dose	Minimum interval 6 months after the first dose
Gardasil® (Quadrivalent)	Females & males 11-26 (min. age 9)		
Gardasil® 9 (nonavalent)	Females & males 11-26 (min. age 9)		

If second and third doses are delayed, there is no need to restart the series. Recommendations for maximal and minimal intervals between each dose are provided in each vaccine's package insert. Cervarix® and Gardasil® are not interchangeable and once the series is started it should be completed with the same vaccine whenever possible. Second and third doses should be given regardless of the amount of time that has passed. Genital tract HPV DNA testing is not recommended to screen female patients for pre-existing HPV infections. Although these vaccines are not recommended for administration to pregnant females, routine pregnancy testing prior to doses is not recommended (see "Precautions" below).

Giving HPV vaccine with other vaccines

- The HPV series can conveniently and safely be initiated in tandem with other vaccines. It is recommended (ACIP, AAP, and AAP) to be given with the other vaccines for 11 or 12 year olds – the Meningococcal Conjugate (MCV4) and the Tetanus, Diphtheria, Pertussis (Tdap) booster.
- HPV vaccine has also been safely administered with Hepatitis B vaccine.

Side effects

Local: injection site pain (80-90%), swelling (25-92%), and erythema 25-45%

Systemic: low grade fever (4%–13 %), headache (12-53%) nausea (4 %) and dizziness (< 3%), fatigue (55%), myalgia, or arthralgia (21-49%) gastrointestinal symptoms (3-27%)

Contraindications

Previous allergic reactions to any of the vaccine constituents.
 Gardasil®: aluminum hydroxyphosphate sulfate, L-histidine, and sodium borate
 Cervarix®: aluminum hydroxide, and sodium dihydrogen phosphate dehydrate, insect cell and bacterial protein. Prefilled syringes contain latex tips and plungers that may cause reactions in latex sensitive individuals.

Precautions

- Successful completion of the HPV vaccine series does not change the recommendations for periodic screening with Pap smears; testing is recommended to be completed according to ACOG guidelines.
- HPV vaccine is not recommended during pregnancy. If a recipient is determined to be pregnant, the series should be interrupted until after parturition. Merck maintains a Pregnancy Registry to monitor fetal outcomes of pregnant women exposed to Gardasil®. Patients and healthcare providers are encouraged to report any exposure to the vaccines during pregnancy by calling 800-986-8999 for Gardasil® or 1-888-452-9622 for Cervarix®; however, the incidence of Cesarean section, pregnancy related problems, and congenital anomalies were equivalent in women receiving HPV vaccines or placebo.
- Because those being vaccinated may develop syncope, observation for 15 minutes is strongly recommended.

How to obtain the vaccine

- Vaccine may be ordered through the Vaccines for Children (VFC) program at the New Mexico Department of Health for all adolescents 11 or 12 years old, and for catch-up vaccination for adolescents ages 13 through 18 years. Use the VFC online ordering system. The New Mexico State purchased vaccines that are available for all New Mexico children can be ordered through the VFC program as well for children who are insured through NM statute, Vaccine Purchase Act (2015).
- Vaccine for other age groups may be obtained at MerckVaccines.com or by calling 1-877-VAX-MERCK (1-877-629-6372) and at GlaxoSmithKline www.gskvaccinesdirect.com or 1-866-475-8222.

Suggestions for smooth third party reimbursement

- Vaccine obtained through VFC (not purchased):** Vaccine is available for order at no charge to the provider through the VFC program for both males and females, 9-18 years of age. No source can be billed for the vaccine acquired from VFC. Claims should show the vaccine code (90649) with a zero (\$0.00) charge and the administration fee code (90471 or 90472). The exception is the fee-for-service, exempt Medicaid (not Centennial) program. For exempt Medicaid providers, use only the CPT code for the vaccine (90649) and enter the usual charge for vaccine administration. Use diagnosis code V05.8 for HPV vaccine and administration.
- Vaccine not obtained through VFC (purchased):** Thanks to the Affordable Care Act and New Mexico statutes, vaccines are mandated to be covered by insurance companies. It is customary to bill for vaccine and vaccine administration. We suggest you place CPT-4 modifier -25 after your evaluation and management code (99201-99215) to indicate the office visit was unrelated to administration of HPV vaccine. Use diagnosis code V05.8 for HPV vaccine and administration.

For additional information

New Mexico Department of Health at www.immunizenm.org 866-681-5872

Pink Book section on Human Papillomavirus (HPV): <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html>

CDC Vaccination Information Statement: <http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hpv-gardasil.html>