**Protocol for Human Papillomavirus 9-valent Vaccine, Recombinant**

**(9vHPV Vaccine, GARDASIL®9)**

**Precautions and Contraindications**

Screen all patients for precautions and contraindications prior to immunization.

**FDA Approved Indications and Usage (See Package Insert, current version dated 1/2017)**

**Girls and Women:**

* The 9-valent human papillomavirus (9vHPV) vaccine **IS INDICATED** in girls and women aged 9 through 26 years of age for the prevention of the following diseases caused by human papillomavirus (HPV) types included in the vaccine:
	+ Genital warts (condyloma acuminata) caused by HPV types 6 and 11.
	+ Cervical, vulvar, vaginal, and anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58.

And [for the prevention of] the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

* + Cervical intraepithelial neoplasia (CIN) grade 2/3 and
	cervical adenocarcinoma *in situ* (AIS).
	+ Cervical intraepithelial neoplasia (CIN) grade 1.
	+ Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3.
	+ Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3.
	+ Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

**Boys and Men:**

* The 9-valent human papillomavirus (9vHPV) vaccine **IS INDICATED** in boys and men
aged 9 through 26 years of age for the prevention of the following diseases:
	+ Genital warts (condyloma acuminata) caused by HPV types 6 and 11.
	+ Anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58.

And [for the prevention of]the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58.

* + Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

**Advisory Committee on Immunization Practices (ACIP) Recommended Schedule\***

* **ROUTINE VACCINATION:** 9vHPV vaccine **IS RECOMMENDED** in a 2-dose series for females aged 11 or 12 years or when initiating at ages 9 through 14 years.
* **ROUTINE VACCINATION:** 9vHPV vaccine is RECOMMENDED in a 2-dose series for males aged 11 or 12 years or when initiating at ages 9 through 14 years. **CATCH-UP VACCINATION**: 9vHPV vaccine **IS RECOMMENDED** for girls and women aged 13 through 26 years, who have not been vaccinated previously or who have not completed the 2-dose series (if initiated at ages 9 through 14 years) or completed the 3-dose series (if initiated at age 15 years or older)
* **CATCH-UP VACCINATION:** 9vHPV vaccine **IS RECOMMENDED** for boys and men aged 13 through 21 years, who have not been vaccinated previously or who have not completed the 2-dose series (if initiated at ages 9 through 14 years) or completed the 3-dose series (if initiated at age 15 years or older). Males aged 22 through 26 years of age may be vaccinated.
* **OTHER VACCINATION:**
	+ The vaccine series may be started at age 9 years for both females and males.
	+ Administer HPV vaccine beginning at age 9 years to children with a history of sexual abuse or assault who have not initiated or completed the series.
* The 9vHPV vaccine **IS RECOMMENDED** in a 3-dose series for immunocompromised persons (as a result of infection [including HIV], disease, or medications) aged 9 through 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series.
* The 9vHPV vaccine **IS RECOMMENDED** for men who have sex with men (MSM) through age 26 years for those who have not been vaccinated previously or who have not completed the series.
* The 9vHPV vaccine **IS RECOMMENDED** for transgender persons as for all adolescents, and initiation of vaccination through age 26 years for those who were not adequately vaccinated previously.
* Eligible females and males (aged 9 through 14 years) given 9vHPV vaccine for routine or catch-up vaccinations should complete a 2-dose series with the following schedule:
	+ 1st dose: At elected date
	+ 2nd dose: 6 through 12 months after the first dose
* Eligible females and males (aged 15 through 26 years of age and immunocompromised persons aged 9 through 26 years) given 9vHPV vaccine for routine or catch-up vaccinations should complete a 3-dose series with the following schedule (Note that this schedule is the same for the 4vHPV vaccine):
* 1st dose: At elected date
* 2nd dose: 1 through 2 months after the first dose
* 3rd dose: 6 months after the first dose

\*ACIP recommends completion of the HPV 3-dose series regardless of the patient’s age (i.e., even if the patient is older than age 26 years) as long as the HPV series was started at age 26 years or younger, [http://www.immunize.org/askexperts/experts\_hpv.asp](http://www.immunize.org/vis/meningococcal_b.pdf).

**Minimum age and minimum (min.) intervals for 9vHPV vaccine

2 doses: Initiating vaccination for children aged 9 through 14 years:**

 Minimum age Min. Interval between

9 years old Dose 1 and 2

 5 months

If a 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.

**3 doses: Initiating vaccination for adolescents and adults aged 15 through 26 years and for immunocompromised persons aged 9 through 26 years:**

Minimum age Min. Interval between Min. Interval between Min. Interval between

 9 years old Dose 1 and 2 Dose 2 and 3 Dose 1 and 3

 4 weeks 12 weeks 24 weeks

\*Doses received after a shorter than recommended dosing interval should be re-administered after another minimum interval has been met since the most recent dose.

**Persons vaccinated previously.**

* Persons who initiated vaccination with 9vHPV, 4vHPV, or 2vHPV before their 15th birthday, and received 2 doses of any HPV vaccine at the recommended dosing schedule (0, 6–12 months), or 3 doses of any HPV vaccine at the recommended dosing schedule (0, 1–2, 6 months), are considered adequately vaccinated.
* Persons who initiated vaccination with 9vHPV, 4vHPV, or 2vHPV on or after their 15th birthday, and received 3 doses of any HPV vaccine at the recommended dosing schedule, are considered adequately vaccinated.
* 9vHPV may be used to continue or complete a vaccination series started with 4vHPV or 2vHPV.
* For persons who have been adequately vaccinated with 2vHPV or 4vHPV, there is no ACIP recommendation regarding additional vaccination with 9vHPV.

**Interrupted Vaccine Schedules:** There is no maximum interval between doses of 9vHPV vaccine. If the vaccine schedule is interrupted, the vaccine series does not need to be restarted. The number of recommended doses is based on age of administration of the first dose.

* In 2 dose series: The first and second doses should be separated by an interval of six to twelve months with a minimum interval of at least 5 months between doses.
* In 3 dose series: The first and second doses should be separated by an interval of at least one month. The second and third does should be separated by an interval of at least 3 months, with a minimum interval of 6 months between the first and third doses.

**Interchangeability of HPV vaccine products (i.e., manufacturer’s brand)**

**Girls and Women:** It was previously recommended that the HPV vaccine series for girls and women be completed with the same HPV vaccine product (i.e., same manufacturer’s brand) whenever possible, as no clinical trials or studies have been published on the efficacy and protection afforded after interchanging HPV vaccine products. After May 2017, only 9vHPV vaccine will be available in LHDs for administration to girls and women,

If vaccination providers do not know the brand of HPV vaccine administered, or do not have available the 2vHPV vaccine or 4vHPV vaccine product previously administered, 9vHPV vaccine product may be used to continue or complete a HPV vaccine series for females.

* The 2vHPV vaccine provided protection only against two HPV types,
i.e., types 16 and 18.
* The 4vHPV vaccine provided protection against four HPV types,
i.e., types 6, 11, 16, and 18.
* The 9vHPV vaccine provides protection against nine HPV types,
i.e., types 6, 11, 16, 18, 31, 33, 45, 52, and 58.

**Interchangeability of HPV vaccine products (i.e., manufacturer’s brand) - Continued**

**Boys and Men:**

After May 2017, only 9vHPV vaccine will be available in LHDs for administration to boys and men.

* + Only 4vHPV or 9vHPV vaccine is FDA approved for administration to boys or men to initiate, continue, or complete the HPV vaccine series.
	+ If vaccination providers do not know the brand of HPV vaccine administered or do not have available the 4vHPV vaccine product previously administered, 9vHPV vaccine product may be used to continue or complete a HPV vaccine series for males.

**Dosage and Route**

* 0.5-mL
* Intramuscular (IM)
* **GARDASIL 9**® is a suspension for intramuscular administration and is available in
0.5-mL single dose vials and prefilled syringes

**Anatomical Site**

* Administer in outer aspect of the deltoid of the upper arm or in the higher anterolateral area of the thigh. As with other intramuscular injections, use with caution in patients on anticoagulant therapy.

**Precautions**

* Prior to administering the vaccine, obtain a vaccination history to determine any reactions to any HPV vaccine including the 9vHPV vaccine.
* Safety of **GARDASIL 9**® has not been shown in pregnant women.
	+ A pregnancy registry is available. Health care providers are encouraged to register women exposed to **GARDASIL 9**® around the time of conception or
	during pregnancy by calling 1-800-986-8999
* Pregnancy – the 9vHPV vaccine **is not recommended** for use in pregnant women. However, pregnancy testing is not needed before vaccination. Receiving HPV vaccine when pregnant is not a reason to consider terminating the pregnancy.
	+ Initiation of the vaccine series should be delayed until after completion of the pregnancy.
	+ If a woman is found to be pregnant after initiating the vaccination series, the remainder of the 3-dose series should be delayed until after completion of the pregnancy.
	+ If a vaccine dose has been administered during pregnancy, no intervention is needed.
* Nursing Mothers
	+ Note: The ACIP recommendations, the contents in the 9vHPV vaccine VIS (dated 03/31/2016) and HPV vaccine VIS (dated 12/02/2016) recommend “Women who are breastfeeding may be vaccinated.” [http://www.immunize.org/vis/hpv\_gardasil\_9.pdf](https://www.gsksource.com/gskprm/htdocs/documents/MENHIBRIX.PDF); differ from the **GARDASIL 9**® Package Insert contents, i.e., “It is not known whether GARDASIL 9 is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **GARDASIL 9**® is administered to a nursing woman.”
* Immunocompromised individual’s response to **GARDASIL 9**® may be diminished.
* Immunosuppression and immunosuppressive therapies – 9vHPV vaccine is not a live vaccine. The 9vHPV vaccine can be administered to females and males who are immunosuppressed by diseases or are receiving immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses). However, the immune response and vaccine efficacy might be less than that in persons who are immunocompetent.

**Warnings**

Observation for 15 minutes after administration of the 9vHPV vaccine is recommended because some persons may develop syncope, sometimes resulting in falling with injury. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following HPV vaccination. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position.

**Contraindications**

**DO NOT** administer 9vHPV vaccine to individuals with:

* A true hypersensitivity, including severe allergic reactions, to common baker’s yeast.
* A history of hypersensitivity or anaphylactic reactions after receiving a previous dose of 4vHPV vaccine or a previous dose of 9vHPV vaccine.
* An allergy to Amorphous Aluminum Hydroxyphosphate Sulfate.
* An allergy to Polysorbate 80.

**Adverse Events**

* See the product’s package insert.
* See Adverse Events Following Vaccinations page of this section.
* Report suspected adverse reactions by contacting Merck Sharp & Dohme Corp.,
a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or
VAERS at 1-800-822-7967 or [http://www.vaers.hhs.gov](http://www.vaers.hhs.gov/)

**Storage and Handling**

* Store in refrigerator at 36oF to 46oF (2oC to 8oC) and **Do Not Freeze.**
* Protect from light.
* Administer 9vHPV vaccine as soon as possible after being removed from refrigeration.
* 9vHPV vaccine can be out of refrigeration (at temperatures at or below 77oF / 25oC) for a total time of not more than 72 hours.
* Shake well before use. Thorough agitation immediately before administration is necessary to maintain suspension of the vaccine. After thorough agitation, 9vHPV vaccine is a white, cloudy liquid.
* Do not use 9vHPV vaccine if particulates are present or it appears discolored.
* 9vHPV vaccine should not be diluted or mixed with other vaccines.

**Other Important Notes**

* Inform the patient, parent, or guardian that administration of **GARDASIL 9**® vaccine does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening.
* Recipients of **GARDASIL 9**® vaccine should not discontinue anal cancer screening if it has been recommended by a health care provider.
* **GARDASIL 9**® has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity.
* **GARDASIL 9**® has not been demonstrated to protect against diseases due to HPV types other than 6, 11, 16, 18, 31, 22, 45, 52, and 58.
* **GARDASIL 9**® is not intended to be used for treatment of active external genital lesions, cervical, vulvar, vaginal, and anal cancers, CIN, VIN, VaIN, or AIN.
* Not all vulvar, vaginal, and anal cancers are caused by HPV, and **GARDASIL 9**® protects only against those vulvar, vaginal, and anal cancers caused by HPV types 16, 18, 31, 22, 45, 52, and 58.
* Vaccination with **GARDASIL 9**® may not result in protection in all vaccine recipients.
* 9vHPV vaccine can be administered to persons with minor acute illnesses. Vaccination of persons with moderate or severe acute illnesses should be deferred until after the patient improves.
* 9vHPV vaccine does not contain preservatives (e.g., thimerosal) or antibiotics.

**References**:

Advisory Committee on Immunization Practices, Vaccines for Children Program, Vaccines to Prevent Human Papillomavirus. VFC Resolution No. 10/16-2

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<https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm>.

Centers for Disease Control and Prevention. Supplemental information and guidance for vaccination providers regarding use of 9-valent HPV vaccine (November 2016).

[https://www.cdc.gov/hpv/downloads/9vhpv-guidance.pdf](https://www.vaccineshoppe.com/image.cfm).

Iverson OE, Miranda MJ, Ulied A, et al. Immunogenicity of the 9-Valent HPV Vaccine Using
2-Dose Regimens in girls and boys vs. a 3-Dose Regimen in Women. JAMA 2016; 316(22);2411-2421. [http://jamanetwork.com](http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM431447.pdf)

Advisory Committee on Immunization Practices, Vaccines for Children Program, Vaccines to Prevent Human Papillomavirus. VFC Resolution No. 02/15-2

[http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/2015-02-2-HPV.pdf](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm)

Petrosky E, Bocchini JA, Hariri S, et al. Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices. MMWR 2015; 64(11): 300-304

[http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6411a3.htm](http://vaers.hhs.gov/helpinstructions)

Centers for Disease Control and Prevention. Supplemental information and guidance for vaccination providers regarding use of 9-valent HPV vaccine (July 2015), [http://www.cdc.gov/hpv/downloads/9vhpv-guidance.pdf](http://vaers.hhs.gov/resources/vaers_form.pdf)

FDA licensure of 9-valent human papillomavirus vaccine to include males aged 16-26 years. December 14, 2015, [http://www.cdc.gov/hpv/downloads/9vhpv-fda.pdf](http://www.cdc.gov/vaccines/programs/vfc/providers/resolutions.html)

**GARDASIL 9**® Package Insert (Dated 1/2017) [http://www.merck.com/product/usa/pi\_circulars/g/gardasil\_9/gardasil\_9\_pi.pdf](https://www.novartisvaccinesdirect.com/PDF/Menveo_Full_Promotional_PI.pdf)

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