Royal College of Obstetricians & Gynaecologists

AICC
All India Co-ordinating Committee

Consensus Paper on Best Practice Recommendations on Mandatory HPV Vaccination in Women of Targeted Age Groups

WELCOME NOTE

Cervical cancer is the fourth leading cause of cancer among women globally and is the second among the cancers that affect Indian women. The quadrivalent (qHPV) vaccine, effective against HPV-6/11/16/18 strains, prevents almost 70% of cervical cancer cases attributable to HPV-16/18 worldwide.

However, the nonavalent (9vHPV) vaccine not only protects against strains (6/11/16/18) that are already covered by the quadrivalent HPV vaccine but also extends its coverage to the following five most common global oncogenic types 31, 33, 45, 52, and 58 in cervical cancer versus the quadrivalent HPV vaccine. The 9vHPV vaccine provides broader protection against cervical cancers caused by* 9 HPV strains *included in* the vaccine.

International organizations strongly recommend primary prevention with the HPV vaccine. FOGSI has endorsed WHO recommendations and rolled out an intensive program to train OBGYNs on HPV vaccination and cervical cancer prevention. There is an increasing public awareness as well.

AICC RCOG is recommitting itself to this cause by coming together and releasing this consensus statement. This document highlights the need to keep the messaging focussed on the prevention of HPV infection for all while paying specific attention to the more vulnerable groups.

I am thankful to all the members of the committee who have helped draft this statement.

Dr. Uma Ram

Dr. Basab Mukherjee

Dr. Sumana Manohar

Dr. Purnima Satoskar

Dr. Anita Kaul

Dr. Samsuzoha

Dr. Sarita Bhalerao

Dr. Anbu Subbian

Dr. Saritha Shamsunder

Dr. Meeta Nakhare

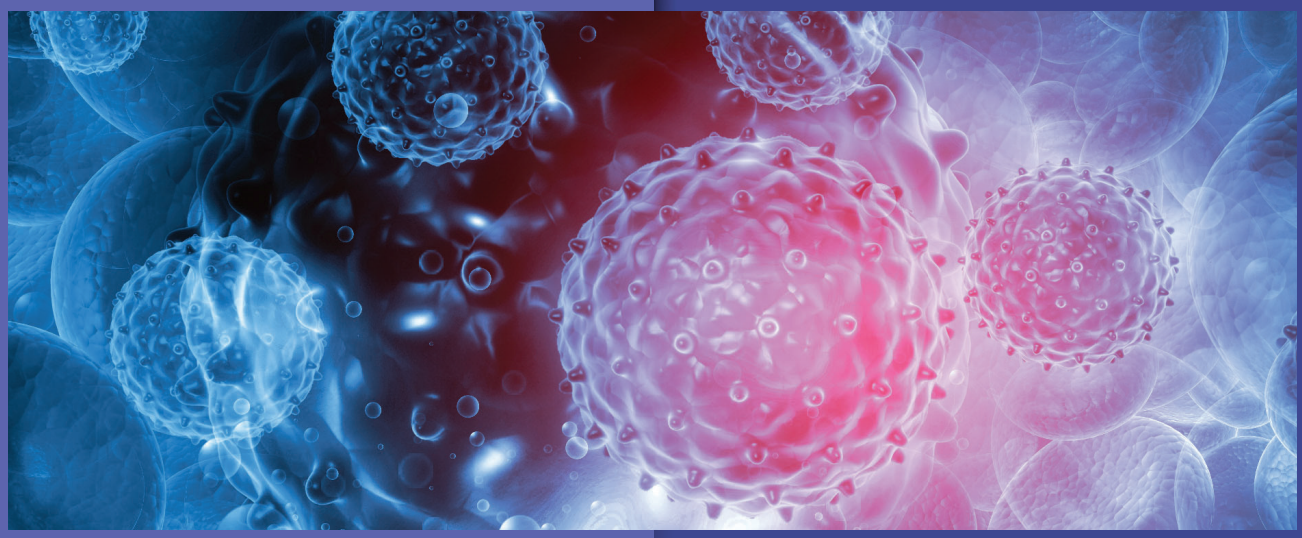
Dr. Seema Sharma

Best Practice Recommendations on Mandatory HPV Vaccination in Women of Targeted Age Groups

EDITORIAL OVERVIEW

Human papillomavirus (HPV) causes cervical, anal, vaginal, vulvar, penile, and oropharyngeal cancers and other diseases like genital warts. Of these, cervical cancer is the most prevalent HPV- related disease, with approximately 99.7% attribution and a leading cause of cancer-related mortality in women worldwide. The correlation between HPV and cervical cancer is notably stronger than the association between smoking and lung cancer (Franco EL_1995). Even with a single partner, as many as half of married women may be at risk of HPV infection and persistence (Burchell AN_2010). The other risk factors associated with HPV infection include early initiation of sexual activity, multiple partners, or intimate skin-to-skin contact. (Panatto D_2012).

While most HPV-induced cervical changes are transient, the development of cervical cancer is contingent on various factors that interact with oncogenic HPV types in the progression toward cancer. Prevention of HPV-related diseases and cancers is crucial due to the significant burden they impose on public health. It is also important to note that all genital HPV infections cannot be entirely prevented except through abstinence and lifetime mutual monogamy. Notably, there is no conclusive evidence that barrier methods such as condom use provide protection against HPV infection, and except for genital warts, the infection is typically asymptomatic. Routine screening through periodic PAP smears has been challenging in susceptible female populations, particularly in developing countries like India. Consequently, vaccination emerges as the most effective form of prevention for both the general as well as at-risk population.



INTRODUCTION

Cervical cancer is the fourth leading cause of cancer among women globally. Human papillomavirus (HPV) types 16 and 18 are accountable for almost 70% of total cervical cancer incidence globally. (Bruni L_2023). It is the second amongst the cancers that affect Indian women, between the age groups of 15-44 years. (Bruni L_2023) Recent data indicate that in India, approximately 123,907 women are diagnosed with HPV cervical cancer each year, with about 77,348 dying from the disease. (Bruni L_2023)

Age is a critical risk factor associated with HPV infection. Adolescents and young adults in the age group of 15 to 25 years are at high risk of being infected with HPV and constitute the majority of fresh infections (75%). This increased risk for infection among younger women has been postulated to be related to the lack of adaptive immune responses and/or the relatively large area of cervical epithelium undergoing squamous metaplasia in this age group, which may enhance the opportunity for HPV DNA to infect the basal cell layer where it can then proliferate. (Dempsey A_2008)

Except for genital warts, the HPV infection is asymptomatic. In 2019, the adherence to cervical cancer screening was at 33.66% worldwide, and was higher in high-income countries (HICs) (75.66) than in low and middle-income countries (LMICs) (24.91). (Zhang W _2022). In a developing country like India, large-scale routine screening is challenging to accomplish. (Kaarthigeyan K_2012)

HPV vaccines are widely recommended to prevent associated infections. The vaccines have been found to be highly effective in reducing HPV infections and related complications, such as genital warts and certain cancers, offering significant protection to individuals who receive them. (Centers for Disease Control and Prevention, “HPV Vaccine Information for Young Women”).

Physicians face hurdles in advocating for HPV vaccination due to national regulations, dosage recommendations, limited practice-level opportunities, costs, and vaccine accessibility. Additionally, hesitancy among parents and caregivers in discussing cervical cancer and prevention hinders advocacy for HPV vaccination amongst preadolescents, adolescents, young adults, sexually active women, and older women. This hesitancy hinders efforts to promote the vaccine. (Kataria I_2022)

The Government of India has recently declared its plan to incorporate HPV vaccines into the national immunization program for girls aged 9-14. These vaccines will be administered at government primary health care centres and schools (Ministry of Finance, Press Release 2024). However, a significant concern arises for adolescents and young adults aged 15 and above who fall outside the scope of the targeted population for government-provided HPV vaccines. This age group is equally crucial for HPV disease prevention and may miss out on the essential protection offered by these vaccines.

Increased susceptibility to HPV-related infections in adolescent females

The transition into adolescence brings a cytological change in the cervical epithelium. The broad zones of columnar epithelial cells evolve into squamous epithelial cells because of heightened vaginal acidity. During the cell transition period, the squamous epithelial cells are highly vulnerable to acquiring lesions with repeated HPV infections of high-risk strains (types 16, 18, 31, 33, 45, 52 and 58 to name a few). Most lesions heal on their own. However, other lesions start to develop when the HPV strains attach to the cellular DNA. It ultimately may progress into cervical intraepithelial neoplasia CIN I, CIN II, and CIN III which correspond to the stages of precancerous lesions in the cervix. (Castle PE 2004, Moscicki AB 2007, Ramachandran D 2021) Infection by established high- risk strains of HPV, environmental or lifestyle factors, and co-infection with viruses increase the chances of HPV-related cervical carcinomas. (Burd EM 2016, Ramachandran D 2021, zur Hausen H 2022). Engaging in sexual activity at a younger age has been linked to approximately twice the risk of developing HPV-related cancers and diseases in later life. (Bruni L 2023)

Vulnerability of early sexual debutants and women with single/multiple partners to HPV infection

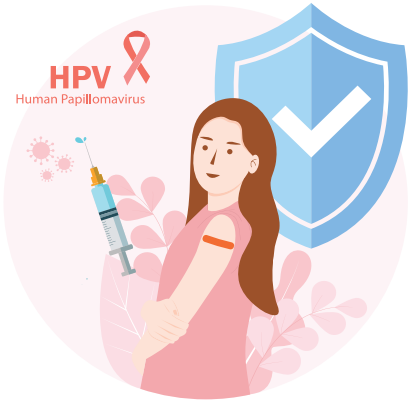
Organizations such as FOGSI (Federation of Obstetric and Gynaecological Societies of India) (FOGSI 2018) and IAP (Indian Academy of Pediatrics) (IAP_2024) have placed significant emphasis on the use of HPV vaccination among preadolescents, adolescents, young adults, and older women in their guidelines. It is important to be aware of and prioritize the sexually active group when advocating for HPV vaccination.

Females who are early sexual debutants, and or having single and multiple sexual partners are also vulnerable to HPV infection. (Mekonnen AG_2023, Louie KS 2009) An Indian study [National Family Health Survey [(NFHS)-5 2019-21] done in 1,10,000 female participants was done in 707 districts, 28 states, and eight union territories. It was reported that in the urban and rural female populations the median first sex ages were 20.2 years and 18.5 years respectively. In an observational study conducted in Brazil, which analyzed 898,921 test results among individuals aged 18 to 34, it was observed that females who initiated intercourse between the ages of 13 to 16 had nearly twice the incidence of high-grade cervical lesions compared to those who began between 17 to 24 years. (Xavier-Júnior 2017)

Research has indicated that sexually active women, irrespective of their relationship status (single, in a relationship, married, or married with children), are susceptible to HPV infection and its persistence. Even with a single partner, as many as half of married women may be at risk of HPV, highlighting the pervasive nature of the virus across different relationship statuses (Burchell AN_2010). This highlights the importance of considering HPV prevention and vaccination strategies for all sexually active women, regardless of their relationship status.

On average in India, women who have engaged in sexual activity report having had approximately 1.7 life-time sexual partners. Similarly, men who have had sexual experiences report an average of 2.1 life-time sexual partners [(NFHS)-5 2019-21]. A meta-analysis has reported that the risk of both malignant and non-malignant cervical disease is relatively stable in women with more than 4-7 sexual partners. (Liu ZC 2015)

Importance of preventing HPV infections through vaccination



- Vaccinating preadolescents and adolescents is crucial as the immune response to the vaccine is stronger at these ages.
- HPV vaccines have proven to constantly induce stable serum antibody responses and sterilizing immunity for over a decade, even without a booster. (Markowitz LE_2021)
- It is recommended to vaccinate individuals before they become sexually active to ensure maximum effectiveness of the vaccine.
- If an individual misses the vaccine during preadolescence and adolescence, it is still essential to prioritize HPV vaccination at the earliest opportunity, as it remains effective in protecting adult women from HPV diseases and infections.
- Achieving high vaccination coverage can lead to herd immunity (Kamolratanakul S 2021), benefiting both vaccinated and unvaccinated individuals in the community.
- HPV vaccination also contributes to overall sexual health by protecting against other HPV related infection besides cervical cancer.
- Additionally, HPV vaccination also offers long-term protection, reducing the risk of developing related diseases and cancers later in life.

Thus, preventing HPV diseases and cancers through vaccination in preadolescents, adolescents, sexually active women and young adults is of utmost importance.

Awareness of HPV and promotion of good sexual practices

Advocating awareness about HPV infection risks, especially in this vulnerable population is a crucial step (Stephens ES 2023). HPV vaccine reluctance is high because of multidimensional socio-cultural, traditional, and religious beliefs and practices (Grandahl M 2018). Hence, there is a dire need to touch upon cultural and social barriers that obstruct honest discussions about sexual health in India.

Community-based awareness have demonstrated improved results. (Panagides R 2023). A study performed at a middle-school level emphasized that text messaging the adolescents might be a smart approach to enhance HPV awareness. (Cates JR 2015). Similarly, school-based programs have shown a drastic increase in and vaccination. (Wong LP 2020)

Barrier methods like condoms offer protection against many sexually transmitted diseases but their effectiveness in preventing HPV infections is not fully established. Research indicates that consistent condom use may reduce the risk of acquiring genital HPV infections and promoting regression of the disease (Pierce Campbell CM 2013). However, certain anatomical sites on the male genitalia, such as the penile shaft, prepuce, glans penis/coronal sulcus, and scrotum, have been identified as having high prevalences of HPV (Giuliano AR 2007), which are not fully covered by condoms. While condoms may not entirely prevent HPV infections, they may offer some level of protection against genital warts, cervical intraepithelial neoplasia (CIN), and invasive cervical cancer (Manhart L 2002).

Regular screening for HPV infections as per standard of practice is important for the early diagnosis of precancerous lesions and prevention. The American Cancer Society recommends starting screening at the beginning of 25 years. (Fontham ETH 2020) FOGSI recommends screening to commence at 25 years in good resource setting and 30 years otherwise (Level 1, Strong

Recommendation) (FOGSI_2023). The common screening tools are a primary HPV test, co-testing (HPV test and cytology), cytology, or Visual Inspection with Acetic Acid (VIA). Newer screening techniques like liquid-based cytology, biomarkers, vaginal self-collection for HPV testing, are also available.

Role of HPV vaccines

Three HPV vaccines—9-valent HPV vaccine and two quadrivalent HPV vaccines are available in India. These HPV vaccines are safe and well tolerated. HPV vaccines have the potential to prevent more than 90% of cancers caused by HPV (caused by the relevant genotypes included in the respective vaccines). (Centers for Disease Control and Prevention, “HPV Vaccine Information for Young Women”).

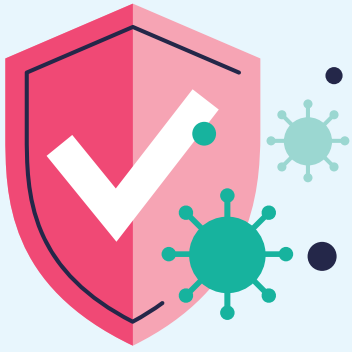
Quadrivalent vaccine

This vaccine protects against 4 HPV strains (6, 11, 16 and 18). Of these, oncogenic HPV types (16 and 18) account for over 70% of cervical cancer cases worldwide. Additionally, the vaccine is effective at preventing precancerous cervical lesions as well as anogenital warts (caused by HPV types 6 and 11). From Indian context quadrivalent HPV vaccines offer 83.2% coverage (Bruni L_2023). They are available as Gardasil (MSD) and Cervavac (Serum Institute of India). Gardasil is indicated for girls and women 9-45 years whereas Cervavac is licensed for girls 9-26 years.

Nonavalent vaccine

This vaccine is available as Gardasil 9 and covers HPV genotypes 6, 11 (non-oncogenic), 16, 18 (oncogenic) which are also present in quadrivalent vaccines in addition to 5 other oncogenic genotypes 31, 33, 45, 52 and 58 thereby offering comprehensive protection against HPV diseases and cancers (98.4% coverage) (Bruni L_2023). This vaccine is indicated for girls and women 9-45 years.

The 9-valent HPV vaccine has been rigorously tested through robust clinical trials spanning over 10 years, demonstrating its safety and tolerability among over 15,000 participants worldwide. It has shown immunogenicity, efficacy, and effectiveness across diverse populations globally. Notably, the vaccine provides the first gender-neutral protection against genotypes responsible for disease burden in boys, girls, and young women in India. Presently, it is included as part of the National Immunization Program in 52 countries worldwide, contributing to potentially saving millions of lives. Additionally, the 9-valent vaccine is cost-effective compared to the quadrivalent vaccine among 12–26-year-old girls (Chesson HW_2016).



Recommended HPV vaccination schedule

(Aligned with FOGSI GCPR 2023)

	Schedule	Evidence level and grade of recommendation
Optimal dose	• Two doses 9–14 years at least 6 months apart • Three doses above 15–26 years (0, 1–2 months, 6 months) • Three doses for older women till 45 years Regular screening as per guidelines has to be followed in this age group	Level I, Grade A Level II, Grade
Reduced dose* • Two doses WHO SAGE • Recommendation • Alternative single dose (Off label)**	• One or two doses for 9–14 years • One or two doses for 15–20 years • Two doses for 21 years and above • Single dose schedule can be used for girls and boys aged 9–20 years	Level II, Grade B Level II, Grade B
Boys	• Boys can be vaccinated from 9–26 years • 9–14 years 2 doses 0, 6 months • 15–26 years 3 doses 0, 2, 6 months	Level II, Grade C

*-Reduced dose schedule of HPV vaccine awaits Drug Controller General of India (DCGI) approval
** - Single dose recommendation is only for quadrivalent HPV vaccine (Gardasil)

Consensus Recommendations

- HPV infections pose a significant disease burden in India, primarily transmitted sexually.
- Prevention of HPV diseases through mandatory vaccination in preadolescents, adolescents, young adults, and even married (single partner) women in India is essential for safeguarding individuals and communities from the potential consequences of HPV infections.
- HPV vaccines have been demonstrated to be safe, immunogenic, effective, and are crucial in reducing the incidence of HPV-related cancers for both girls and boys.
- Long-term data spanning 10-14 years supports the efficacy of the qHPV vaccine (Gardasil) and the 9vHPV vaccine (Gardasil 9).
- While both screening and vaccination are valuable interventions for reducing HPV diseases, it is not imperative to conduct screening before administering the vaccine. However, there are recommendations that conducting HPV-based screening twice during a person's life at the ages of 35 and 45 can enhance preventive measures (Simms KT_2019).
- Counselling, spreading awareness to educate the target population, and promoting the use of barrier methods such as condoms can complement vaccination efforts to further reduce the risk of HPV diseases.

The AICC RCOG supports HPV vaccination and advocates for its accessibility to all eligible individuals, as this represents a crucial step toward the prevention and control of HPV diseases in India.

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PRIORITIZE WOMEN'S PROTECTION THROUGH HPV VACCINATION

MSD

Image for representation purpose only

~3 out of 10 women are at risk of an high-risk HPV infection after childbirth[1]

1 out of 2 women may be at risk of HPV even with a single partner[2]

HPV-related cervical cancer can strike at one of the most productive periods of a woman's life at the median age of around 38 years[3]

HPV vaccination helps offer ~98% effectiveness* against cervical cancer[4,5]

GARDASIL® [Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Recombinant Vaccine]

GARDASIL®9 Human Papillomavirus 9-valent Vaccine, Recombinant

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SELECTED SAFETY INFORMATION

Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant

GARDASIL® (Suspension for intramuscular injection) **Contraindications:** Hypersensitivity to the active substances or to any of the excipients of the vaccine including severe allergic reactions to yeast (a vaccine component). **Warning and Precautions:** GARDASIL vaccine is not intended to be used for treatment of active external genital lesions; cervical, vulvar, or vaginal cancers; CIN, VIN, VaIN. This vaccine will not protect against diseases that are not caused by HPV. As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of the symptoms and their etiology. Individuals with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may have reduced antibody response to active immunization. This vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. Syncope, sometimes associated with tonic clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL. **Use in special population:** Pregnancy: Pregnancy should be avoided during the vaccination regimen for GARDASIL. Nursing Mothers: GARDASIL may be administered in lactating women. It is not known whether vaccine antigens or antibodies induced by the vaccine are excreted in human milk. Pediatric Use: The safety and efficacy of GARDASIL have not been evaluated in children younger than 9 years. Elderly and HIV-infected individuals: The safety and efficacy of GARDASIL have not been evaluated in elderly and HIV-infected individuals. Drug Interactions: **Use with other Vaccines:** GARDASIL may be administered concomitantly (at a separate injection site) with H-B-VAX II™ [hepatitis B vaccine (recombinant)], Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine], Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)], and Repevax [Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) Vaccine, (adsorbed, reduced antigen(s) content)]. Use with Hormonal Contraceptives: Use of hormonal contraceptives did not appear to affect the immune responses to GARDASIL. Use with Steroids: Use with Steroids did not appear to affect the immune responses to GARDASIL. **Undesirable Effects:** The vaccine-related adverse experiences that were observed among recipients of GARDASIL at a frequency of at least 1%. Vaccine-Related Clinical Adverse Experiences in 9- Through 45-Year-Old Girls and Women are headache, dizziness, nausea, pain in extremity, pyrexia. Most of the adverse experiences seen with concomitant administration with other vaccines were reported as being mild to moderate in intensity. Undesirable effects as per Post-Marketing reports were cellulitis, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, lymphadenopathy, pulmonary embolus, acute disseminated encephalomyelitis, dizziness, Guillain-Barre syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonic-clonic movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis, deep venous thrombosis, nausea, pancreatitis, vomiting, arthralgia, myalgia, asthenia, chills, death, fatigue, malaise, Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

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HUMAN PAPILLOMAVIRUS 9-VALENT VACCINE, RECOMBINANT [Serotype 6 L1, 11 L1, 16 L1, 18 L1, 31 L1, 33 L1, 45 L1, 52 L1 & 58 L1]

GARDASIL® 9 (Suspension for intramuscular injection) **Contraindications:** GARDASIL 9 is contraindicated in patients with hypersensitivity to either GARDASIL 9 or any of the inactive ingredients in either vaccine.

Warning and Precautions: GARDASIL 9 vaccine is not intended to be used for treatment of active external genital lesions; cervical, vulvar, vaginal, or anal cancers; CIN, VIN, VaIN, or AIN. This vaccine will not protect against diseases that are not caused by HPV. As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. Syncope (fainting) may follow any vaccination, especially in adolescents and young adults. The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of the symptoms and their etiology. Individuals with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may have reduced antibody response to active immunization. This vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. **Use in special population:** Pregnancy: Pregnancy should be avoided during the vaccination regimen for GARDASIL 9. Nursing Mothers: GARDASIL 9 may be administered in lactating women. It is not known whether vaccine antigens or antibodies induced by the vaccine are excreted in human milk. Pediatric Use: The safety and efficacy of GARDASIL 9 have not been evaluated in children younger than 9 years. Immunocompromised Individuals: The immunologic response to GARDASIL 9 may be diminished in immunocompromised individuals. **Drug interactions: Use with other Vaccines:** GARDASIL 9 may be administered concomitantly (at a separate injection site) with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine], Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)], and Repevax [Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) Vaccine, (adsorbed, reduced antigen(s) content)] (dTap-IPV). Use with Hormonal Contraceptives: Use of hormonal contraceptives did not appear to affect the type specific immune responses to GARDASIL 9. Use with Steroids: Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune responses to vaccines. **Undesirable Effects:** The vaccine-related adverse experiences that were observed among recipients of either GARDASIL 9 or GARDASIL at a frequency of at least 1%. Few individuals (GARDASIL 9 = 0.1% vs. GARDASIL <0.1%) discontinued due to adverse experiences after receiving either vaccine. The safety profile was similar between GARDASIL 9 and GARDASIL in women and girls and boys. Solicited Systemic and Injection-Site Adverse Reactions: Temperature and injection-site pain, swelling, and erythema were solicited using VRC-aided surveillance for 5 days after each injection of GARDASIL 9 during the clinical studies. Undesirable effects as per post-Marketing reports were cellulitis, idiopathic thrombocytopenic purpura, lymphadenopathy, acute disseminated encephalomyelitis, dizziness, Guillain-Barré syndrome, headache, syncope sometimes accompanied by tonic-clonic movements, nausea, vomiting, arthralgia, myalgia, asthenia, chills, fatigue, malaise, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

Before prescribing, please consult the full prescribing information.

Scan the QR code for Prescribing Information

HPV: Human papillomavirus; AIN: Anal intraepithelial neoplasia

AE Reporting

To report Adverse Events (AEs) related to our products, please contact :

Mode of reporting the adverse event	Details
PV Dedicated Fax	91-124-4647339
PV Toll Free Number	18001032642
E-mail	dpoc_india@merck.com
Postal Address	International Pharmacovigilance Department, MSD Pharmaceuticals Pvt. Ltd., 6th Floor, Vatika Towers-B, Sector-54, Gurgaon-122002.

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MSD

POSTPARTUM WOMEN ARE AT AN INCREASED RISK OF HPV*,[1] INFECTION AND IT IS ONE OF THE OPPORTUNITIES FOR HPV VACCINATION†,[2]

Opportunity for HPV vaccination in young women after their first delivery[3]

Only **0.4% women aged 24-45 years** are infected with all 4 **HPV serotypes**[4]

>99% of women can still get full benefit from **HPV vaccination**[4]

YOUR STRONG RECOMMENDATION MAY HELP TO SAVE LAKHS OF WOMEN FROM HPV-RELATED CANCERS[5]

GARDASIL®
[Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Recombinant Vaccine]

GARDASIL® 9
Human Papillomavirus 9-valent Vaccine, Recombinant

Why Wait?
Vaccinate Today!

*31% risk. †Quadrivalent HPV vaccine. HPV: Human papillomavirus

References: 1. Nobbenhuis MA, Helmerhorst TJ, van den Brule AJ, et al. High-risk human papillomavirus clearance in pregnant women: trends for lower clearance during pregnancy with a catch-up postpartum. Br J Cancer. 2002;87(1):75-80; 2. CY, Tseng CJ, Chang CC, et al. Postpartum HPV Vaccination Rate and Differences in Background Characteristics Between HPV Vaccinated and Unvaccinated Postpartum Women: Strict Monitoring and Follow-Up of Postpartum HPV Vaccination Program. Front Immunol. 2021;12:626582; 3. Rama CH, Villa LL, Pagliusi S, et al. Opportunity for catch-up HPV vaccination in young women after first delivery. J Epidemiol Community Health. 2010;64(7):610-5; 4. Velicer C, Zhu X, Vuocolo S, et al. Prevalence and incidence of HPV genital infection in women. Sex Transm Dis. 2009 Nov;36(11):696-703. 5. Seth S, Malhotra N, Malhotra J. HPV vaccination—An update. In: Sekaran SK, Patel M, Suman A, et al. (eds.) FOGSIs Update in Obstetrics and Gynaecology. Volume 2. Evangel Publishing, 2022. pp. 165-174.

SELECTED SAFETY INFORMATION

Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant

GARDASIL® (Suspension for intramuscular injection) **Contraindications:** Hypersensitivity to the active substances or to any of the excipients of the vaccine including severe allergic reactions to yeast (a vaccine component). **Warning and Precautions:** GARDASIL vaccine is not intended to be used for treatment of active external genital lesions; cervical, vulvar, or vaginal cancers; CIN, VIN, VaIN. This vaccine will not protect against diseases that are not caused by HPV. As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of the symptoms and their etiology. Individuals with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may have reduced antibody response to active immunization. This vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. Syncope, sometimes associated with tonic clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL. **Use in special population:** Pregnancy: Pregnancy should be avoided during the vaccination regimen for GARDASIL. Nursing Mothers: GARDASIL may be administered in lactating women. It is not known whether vaccine antigens or antibodies induced by the vaccine are excreted in human milk. Pediatric Use: The safety and efficacy of GARDASIL have not been evaluated in children younger than 9 years. Elderly and HIV-infected individuals: The safety and efficacy of GARDASIL have not been evaluated in elderly and HIV-infected individuals. Drug Interactions: **Use with other Vaccines:** GARDASIL may be administered concomitantly (at a separate injection site) with H-B-VAX II™ [hepatitis B vaccine (recombinant)], Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine], Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)], and Repevax [Diphtheria, Tetanus, Pertussis (acellular, component) and Poliomyelitis (inactivated) Vaccine, (adsorbed, reduced antigen(s) content)]. Use with Hormonal Contraceptives: Use of hormonal contraceptives did not appear to affect the immune responses to GARDASIL. Use with Steroids: Use with Steroids did not appear to affect the immune responses to GARDASIL. **Undesirable Effects:** The vaccine-related adverse experiences that were observed among recipients of GARDASIL at a frequency of at least 1%. Vaccine-Related Clinical Adverse Experiences in 9- Through 45-Year-Old Girls and Women are headache, dizziness, nausea, pain in extremity, pyrexia. Most of the adverse experiences seen with concomitant administration with other vaccines were reported as being mild to moderate in intensity. Undesirable effects as per Post-Marketing reports were cellulitis, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, lymphadenopathy, pulmonary embolus, acute disseminated encephalomyelitis, dizziness, Guillain-Barre syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonic-clonic movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis, deep venous thrombosis, nausea, pancreatitis, vomiting, arthralgia, myalgia, asthenia, chills, death, fatigue, malaise, Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.
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