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### **FDA Approves Expanded Age Indication for GARDASIL® 9 in Women and Men Ages 27 through 45 for the Prevention of Certain HPV-Related Cancers and Diseases**

#### **GARDASIL 9 Now Indicated for People Ages 9 through 45**

KENILWORTH, N.J., Oct. 29, 2018 -- The U.S. Food and Drug Administration (FDA) approved an expanded age indication for GARDASIL® 9 (Human Papillomavirus 9-valent Vaccine, Recombinant), Merck's 9-valent HPV vaccine, for use in women and men ages 27 through 45. With this expanded age indication, GARDASIL 9 is now indicated in females 9 through 45 years of age for the prevention of cervical, vulvar, vaginal, and anal cancers caused by HPV types 16, 18, 31, 33, 45, 52, and 58, precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, and genital warts caused by HPV types 6 and 11. GARDASIL 9 is now also indicated in males 9 through 45 years of age for the prevention of anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58, precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, and genital warts caused by HPV types 6 and 11.

GARDASIL 9 is contraindicated in individuals with hypersensitivity, including severe allergic reactions to yeast, or after a previous dose of GARDASIL 9 or GARDASIL® [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant].

"Almost half of the new HPV infections in the United States occur in adults 25 years of age and older, which may put them at risk for certain cancers and diseases," said Anna Giuliano, Ph.D., Dorothea Bennett Memorial – American Cancer Society Clinical Research Professor and Director of the Center for Immunization and Infection Research in Cancer at Moffitt Cancer Center. "Even though adults may have already been exposed to some types of HPV covered by the vaccine, GARDASIL 9 may help protect against certain cancers

and diseases caused by any of the nine HPV types to which someone has not been exposed.”

GARDASIL 9 helps provide protection against certain cancers and other diseases caused by nine HPV types that cause the majority of HPV-related cancers and other diseases in women and men. Worldwide, seven HPV types in GARDASIL 9 (HPV 16, 18, 31, 33, 45, 52 and 58) cause:

- approximately 90 percent of cervical cancer cases;
- approximately 80 percent of high-grade cervical lesions (cervical precancers, defined as CIN 2, CIN 3, and AIS);
- 90 percent of HPV-related vulvar cancers;
- 85 percent of HPV-related vaginal cancers;
- 90 percent of HPV-related anal cancers.

Worldwide, HPV types 6 and 11 cause approximately 90 percent of genital warts cases in males and females. In addition, approximately 50 percent of cases of low-grade cervical lesions (CIN 1) are caused by the nine HPV types covered by the vaccine.

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 16, 18, 31, 33, 45, 52 and 58. GARDASIL 9 is not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; or cervical intraepithelial neoplasia (CIN), vulvar intraepithelial neoplasia (VIN), vaginal intraepithelial neoplasia (VaIN), or anal intraepithelial neoplasia (AIN).

“Routine vaccination for males and females ages 11-12 continues to be recommended by the Centers for Disease Control and Prevention, and now there is an opportunity to vaccinate appropriate men and women through age 45,” said Alain Luxembourg, M.D., Ph.D., director, clinical research, Merck Research Laboratories. “We hope this expanded age indication will help further reduce the number of women and men affected by certain HPV-related cancers and diseases.”

### **Data supporting use of GARDASIL 9 for adults 27 through 45 years of age**

The indication for use of GARDASIL 9 in people ages 27 through 45 is supported by clinical trial data, including:

- Data from the phase 3 clinical trial for GARDASIL in 3,253 women 27 through 45 years of age (FUTURE 3, base study), which showed that a 3-dose regimen in the per-protocol study population was 87.7 percent effective in preventing the

combined incidence of HPV 6/11/16/18-related persistent infection, genital warts, VIN, VaIN, vulvar cancer, vaginal cancer, cervical dysplasia (any grade CIN), AIS and cervical cancer (95% CI: 75.4%, 94.6%) and 95 percent effective in preventing the combined incidence of HPV6/11/16/18-related genital warts or cervical dysplasia (low-grade cervical pre-cancers) (95% CI: 68.7%, 99.9%) through a median duration of 3.5 years of follow-up after receipt of the third dose.

- Data from the long-term follow-up extension study with GARDASIL in 600 women ages 27 through 45 that continued for 10 years following enrollment in the phase 3 base study (FUTURE 3). During the follow-up period from this long-term study, there was sustained effectiveness for up to 10.1 years following vaccination (median 8.9 years); no cases of HPV disease (HPV6/11/16/18- related CIN of any grade or genital warts) were observed in trial participants who were vaccinated during the base study.
- Effectiveness of GARDASIL in men 27 through 45 years of age is inferred from efficacy data in women 27 through 45 years of age and supported by immunogenicity data from a clinical trial in which 150 men, 27 through 45 years of age, received a 3-dose regimen of GARDASIL (0, 2, 6 months).

Nationally representative National Health and Nutrition Examination Survey (NHANES) data from the 2005-2006 survey years were recently published and approximately 17.5 percent of the women participating in this survey were seropositive for two or more of the nine HPV types.

Efficacy, effectiveness, and safety of GARDASIL are relevant to GARDASIL 9 because the vaccines are manufactured similarly and contain four of the same HPV L1 virus-like particles (HPV types 6, 11, 16, and 18). Clinical trials have demonstrated consistent safety, efficacy, and immunogenicity between GARDASIL and GARDASIL 9.

### **Important information about GARDASIL 9**

GARDASIL 9 does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Recipients of GARDASIL 9 should not discontinue anal cancer screening if it has been recommended by a health care professional.

GARDASIL 9 has not been demonstrated to provide protection against diseases from vaccine HPV types to which a person has previously been exposed through sexual activity.

GARDASIL 9 is not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; or cervical intraepithelial neoplasia (CIN), vulvar intraepithelial neoplasia (VIN), vaginal intraepithelial neoplasia (VaIN), or anal intraepithelial neoplasia (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 16, 18, 31, 33, 45, 52, and 58.

Vaccination with GARDASIL 9 may not result in protection in all vaccine recipients.

### **Select Safety Information for GARDASIL 9**

GARDASIL 9 is contraindicated in individuals with hypersensitivity, including severe allergic reactions to yeast, or after a previous dose of GARDASIL 9 or GARDASIL.

Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. 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.

Safety and effectiveness of GARDASIL 9 have not been established in pregnant women.

The most common ( $\geq 10\%$ ) local and systemic adverse reactions in females were injection-site pain, swelling, erythema, and headache. The most common ( $\geq 10\%$ ) local and systemic reactions in males were injection-site pain, swelling, and erythema.

The duration of immunity of GARDASIL 9 has not been established.

### **Dosage and administration for GARDASIL 9**

GARDASIL 9 should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.

- For individuals 9 through 14 years of age, GARDASIL 9 can be administered using a 2-dose or 3-dose schedule. For the 2-dose schedule, the second dose should be administered 6-12 months after the first dose. If the second dose is administered less than 5 months after the first dose, a third dose should be given

at least 4 months after the second dose. For the 3-dose schedule, GARDASIL 9 should be administered at 0, 2 months, and 6 months.

- For individuals 15 through 45 years of age, GARDASIL 9 is administered using a 3-dose schedule at 0, 2 months, and 6 months.

### **About HPV and HPV-related cancers and diseases**

In the United States, human papillomavirus (HPV) will infect most sexually active males and females in their lifetime. According to the CDC, there are approximately 14 million new genital HPV infections in the United States each year, with roughly half occurring in people 25 years of age and older. For most people, HPV clears on its own, but for others who don't clear the virus it could lead to certain cancers and other diseases. Studies suggest that sexually active adults remain at risk for acquiring new HPV infections, and for men in particular, the rate of new infection remains relatively constant, irrespective of age. There is no way to predict who will or won't clear the virus.

Each year in the United States, approximately 26,100 men and women are diagnosed with certain HPV-related cancers. HPV causes virtually all cervical cancer cases. Each day, about 36 women are diagnosed with cervical cancer -- about 13,200 women per year. It is estimated that approximately half of all cervical cancer cases are caused by HPV infections acquired after the age of 20.

Worldwide, HPV also causes approximately 70-75 percent of vaginal cancer cases and approximately 30 percent of vulvar cancer cases in females, and approximately 85-90 percent of anal cancers and all cases of genital warts in both females and males. Persistent HPV infection can lead to abnormal Pap results that may require additional follow-up procedures. Anal cancer and genital warts affect both men and women. According to the American Cancer Society, an estimated 2,960 men and 5,620 women in the United States will be diagnosed with anal cancer in 2018, and overall rates have been increasing. There is no routine screening recommended for the general population to reduce the risk of anal cancer.

Approximately 355,000 cases of genital warts occur each year in the United States, and one study in Brazil published in 2017 showed that the incidence of genital warts in men 31-44 years old was similar to men ages 18-30. Treatment of genital warts can be painful, and they can recur after treatment, especially in the first three months. Approximately 3 out of 4 people get them after having genital contact with someone who has genital warts.

## **About Merck**

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

## **Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA**

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

**Please see Prescribing Information for GARDASIL®9 (Human Papillomavirus 9-valent Vaccine, Recombinant) at [http://www.merck.com/product/usa/pi\\_circulars/g/gardasil\\_9/gardasil\\_9\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf).**

**The Patient Product Information for GARDASIL 9 is also available at [http://www.merck.com/product/usa/pi\\_circulars/g/gardasil\\_9/gardasil\\_9\\_ppi.pdf](http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_ppi.pdf).**

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