



EUROPEAN MEDICINES AGENCY  
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## EPAR summary for the public

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# Gardasil 9

human papillomavirus 9-valent vaccine (recombinant, adsorbed)

This is a summary of the European public assessment report (EPAR) for Gardasil 9. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Gardasil 9.

For practical information about using Gardasil 9, patients should read the package leaflet or contact their doctor or pharmacist.

## What is Gardasil 9 and what is it used for?

Gardasil 9 is a vaccine used in males and females from the age of nine years to protect against the following conditions caused by nine types of the human papillomavirus (HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58):

- precancerous lesions (growths) and cancers in the cervix, vulva or vagina and anus;
- genital warts.

Gardasil 9 is given according to official recommendations. It contains purified proteins from the nine types of HPV listed above.

## How is Gardasil 9 used?

Gardasil 9 is a suspension for injection available in vials or prefilled syringes. Gardasil 9 is normally given according to either a two-dose schedule or a three-dose schedule for males and females from 9 to 14 years old and a three-dose schedule for males and females 15 years old and over. For a two-dose schedule, the second dose should be given between five and thirteen months after the first dose. For a three-dose schedule, the second dose should be given two months after the first and the third given four months after the second. There should always be at least one month between the first and



the second doses, and at least three months between the second and the third, and all doses should be given within a year.

It is recommended that individuals who receive the first dose of Gardasil 9 should complete the dosing regimen using this medicine. The vaccine is given as an injection into a muscle, preferably in the shoulder or the thigh.

The vaccine can only be obtained with a prescription.

## **How does Gardasil 9 work?**

Human papillomaviruses are viruses that cause warts and abnormal tissue growth. There are more than 100 types of papillomavirus, some of which are associated with anogenital cancers in both men and women. Nearly 100% of cervical cancers are caused by HPV infection. In Europe, approximately 90% of anal cancers, 15% of vulvar cancers, 70% of vaginal cancers, and 30 to 40% of penile cancers are estimated to be caused by HPV infection. HPV types 16 and 18 cause a large majority of cervical and anal cancers, while HPV types 6 and 11 cause most of genital warts. A further 5 HPV types (31, 33, 45, 52, and 58) also carry a high risk for developing cancer (they cause around 20% of cervical cancers).

All papillomaviruses have a shell, or 'capsid', that is made up of proteins called 'L1 proteins'. Gardasil 9 contains the purified L1 proteins for the nine HPV types above, produced by a method known as 'recombinant DNA technology'. The proteins are assembled in 'virus-like particles' (structures that look like HPV, so that the body can recognise them easily). These virus-like particles are not capable of causing infection or disease.

When a patient is given the vaccine, the immune system makes antibodies against the L1 proteins. After vaccination, the immune system is able to produce antibodies more quickly when it is exposed to the real viruses. This will help to protect against the diseases caused by these viruses.

The vaccine also contains an 'adjuvant', a compound containing aluminium to stimulate a better response.

## **What benefits of Gardasil 9 have been shown in studies?**

Gardasil 9 can provide protection against all nine types of HPV infection, as seen in five main studies.

The first study looked at the effectiveness of Gardasil 9 in over 14,000 women aged between 16 and 26 years. The study looked at how many women given Gardasil 9 developed disease (growths or cancer) due to HPV infection caused by HPV types 31, 33, 45, 52 and 58 when compared with Gardasil vaccine (a previously approved vaccine which protects against types 6, 11, 16 and 18). This study showed that 1 out of 6,016 women vaccinated with 3 doses of Gardasil 9 developed disease related to HPV types 31, 33, 45, 52 and 58, compared with 30 out of 6,017 women vaccinated with 3 doses of Gardasil. This study also showed that antibody levels against types 6, 11, 16 and 18 were adequate to protect against these four types of HPV infection. The women were followed up for around three and a half years after the third dose of the vaccine.

The second study in 3066 subjects compared the effect of Gardasil 9 in girls and boys aged nine to 15 years with the effect of Gardasil 9 in young women aged 16 to 26 years. The main measure of effectiveness was the development of antibodies against HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 one month after the third dose. The study showed that the vaccine stimulates the production of adequate levels of antibodies against HPV of all nine types in girls and boys aged between nine and 15 years when compared with women 16-26 years of age, for whom protection against disease was demonstrated in the first study.

The third study compared the effect of Gardasil 9 with the effect of Gardasil in 600 girls aged 9 to 15 years. The study looked at the development of antibodies one month after the third dose, and it showed that girls vaccinated with Gardasil 9 have similar levels of protection against types 6, 11, 16 and 18 as girls vaccinated with Gardasil.

The fourth main study compared the levels of antibodies against all nine HPV types one month after the third dose in around 1,419 young men aged 16 to 26 with those in 1,101 women aged 16 to 26. This study found that Gardasil 9 stimulates similar levels of protection against all nine virus types in young men and women.

The fifth main study involving 1,518 subjects compared the effect of a two-dose schedule of Gardasil 9 with a three-dose schedule. This study looked at the development of antibodies one month after the last dose, and it showed that boys and girls given two doses of Gardasil 9 have similar levels of protection against all nine virus types to girls and women given three doses of Gardasil 9.

### **What are the risks associated with Gardasil 9?**

In studies, the most common side effects with Gardasil 9 (seen in more than 1 patient in 10) were reactions at the site of the injection (redness, pain and swelling) and headache. These side effects were normally mild or moderate. For the full list of all side effects reported with Gardasil 9, see the package leaflet.

Patients who show signs of an allergy after a dose of Gardasil 9 (or of its precursor vaccines Gardasil or Silgard) should stop the vaccination course or should not receive Gardasil 9 at all. For the full list of all restrictions, see the package leaflet.

### **Why is Gardasil 9 approved?**

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Gardasil 9's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP considered that Gardasil 9 offers a broader protection against cancer than its precursor Gardasil, since it protects against additional 5 new types of HPV (31, 33, 45, 52 and 58), which although less common than types 16 and 18, are also considered high-risk HPV types. Thus Gardasil 9 is expected to prevent the majority of cervical, vaginal and vulvar cancers and premalignant lesions, as well as genital warts associated with HPV. Regarding side effects, although a large proportion of subjects develop injection site reactions, these are only slightly more than for Gardasil.

### **What measures are being taken to ensure the safe and effective use of Gardasil 9?**

A risk management plan has been developed to ensure that Gardasil 9 is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Gardasil 9, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the [summary of the risk management plan](#).

### **Other information about Gardasil 9**

The European Commission granted a marketing authorisation valid throughout the European Union for Gardasil 9 on 10 June 2015.

The full EPAR and risk management plan summary for Gardasil 9 can be found on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European public assessment reports](http://ema.europa.eu/Find%20medicine/Human%20medicines/European%20public%20assessment%20reports). For more information about treatment with Gardasil 9, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 03-2016.