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**EPAR summary for the public**

# Gardasil

human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)

This document is a summary of the European public assessment report (EPAR) for Gardasil. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Gardasil.

## What is Gardasil?

Gardasil is a vaccine. It is a suspension for injection that contains purified proteins for four types of the human papillomavirus (types 6, 11, 16 and 18). It is available in vials or prefilled syringes.

## What is Gardasil used for?

Gardasil is used in males and females from the age of nine years to protect against the following conditions caused by specific types of human papillomavirus (HPV):

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

Gardasil is given according to official recommendations.

The vaccine can only be obtained with a prescription.

## How is Gardasil used?

For people aged nine to thirteen years, Gardasil can be given as two doses six months apart. If the second dose is given earlier than six months after the first dose, a third dose should always be given. For people aged fourteen or above, Gardasil is normally given according to a three-dose schedule with

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
**E-mail** info@ema.europa.eu **Website** www.ema.europa.eu
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the second dose given two months after the first and the third given four months after the second. These same three doses can also be used in individuals aged nine to thirteen years.

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 should complete the dosing regimen with Gardasil. The vaccine is given as an injection into a muscle, preferably in the shoulder or the thigh.

## How does Gardasil 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 genital cancers. HPV types 16 and 18 cause approximately 70% of cervical cancers and between 75 and 80% of anal cancers. HPV types 6 and 11 cause approximately 90% of genital warts.

All papillomaviruses have a shell, or 'capsid', that is made up of proteins called 'L1 proteins'. Gardasil contains the purified L1 proteins for HPV types 6, 11, 16 and 18, which are produced by a method known as 'recombinant DNA technology': they are made by yeast cells into which a gene (DNA) has been introduced that makes them able to produce the L1 proteins. 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.

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.

## How has Gardasil been studied?

In four main studies of Gardasil given as three dose, Gardasil was compared with placebo (a dummy vaccine) in almost 21,000 women aged between 16 and 26 years. The studies looked at how many women developed genital lesions or warts that were due to HPV infection. The women were followed up for around three years after the third dose of the vaccine.

Three studies of Gardasil given as three doses looked at the ability of Gardasil to prevent infection with HPV types 6, 11, 16 and 18 and genital warts caused by these HPV types in almost 4,000 women aged between 24 and 45 years, and at the development of antibodies against these HPV types in around 1,700 girls and boys aged between nine and 15 years.

Another study in around 800 girls and women compared the effect of two doses of Gardasil in girls aged nine to 13 years with the effect of three doses in girls and young women aged 16 to 24 years. The main measure of effectiveness was the development of antibodies against HPV types 6, 11, 16 and 18 one month after the last dose.

Finally, a main study in around 4,000 boys and men from 16 years of age compared the vaccine with placebo to test the vaccine's effect in preventing genital warts, precancerous anal lesions and anal cancer.

## What benefit has Gardasil shown during the studies?

In the four studies in 21,000 women, out of the more than 8,000 women vaccinated with Gardasil who had never been infected by HPV types 6, 11, 16 or 18 before, one woman developed a precancerous lesion in the cervix that might have been due to HPV type 16 or 18. In contrast, 85 of the more than 8,000 women who received the placebo vaccine developed lesions that were due to these two HPV types. A similar effect of Gardasil was seen when the analysis also included lesions of the cervix due to the other two HPV types (types 6 and 11).

In the three studies on genital warts, 2 women out of almost 8,000 in the Gardasil group developed genital warts, and there were no cases of precancerous lesions of the vulva or the vagina. In contrast, there was a total of 189 cases of external genital lesions out of almost 8,000 women in the placebo group. The studies also showed that Gardasil provided some protection against lesions in the cervix linked to other cancer-causing types of HPV, including type 31. In addition, these studies confirmed the ability of Gardasil to protect against lesions and HPV infection in 24- to 45-year-old women. The studies also showed that the vaccine stimulates the production of sufficient amounts of antibodies against HPV in girls and boys aged between nine and 15 years.

The study testing Gardasil given as 2 doses in girls aged 9 to 13 showed that that the two doses given six months apart were no less effective than the three-dose vaccination: all subjects had developed sufficient amounts of antibodies against HPV one month after their last dose.

In the study boys and men, there were 3 cases genital lesions among around 1,400 patients given the vaccines compared with 32 cases among around 1,400 given placebo. With regard to precancerous anal lesions, there 5 cases in the vaccinated group (consisting of around 200 patients) compared with 24 cases in the placebo group (which also had around 200 patients). There were no cases of anal cancer in the study but it is expected that protection against precancerous anal lesions will translate into protection against the cancer.

## What is the risk associated with Gardasil?

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

Patients who show signs of an allergy after a dose of Gardasil should not receive further doses of the vaccine. Vaccination should be postponed in patients who are ill with a high fever. For the full list of all restrictions, see the package leaflet.

## Why has Gardasil been approved?

The CHMP decided that Gardasil's benefits are greater than its risks and recommended that it be given marketing authorisation.

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

A risk management plan has been developed to ensure that Gardasil 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, including the appropriate precautions to be followed by healthcare professionals and patients.

## Other information about Gardasil:

The European Commission granted a marketing authorisation valid throughout the European Union for Gardasil on 20 September 2006.

The full EPAR for Gardasil can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Gardasil, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2014.