



Public Health  
England

Protecting and improving the nation's health

# HPV vaccination pilot for men who have sex with men (MSM) 2016

Information for healthcare professionals

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## About Public Health England

Public Health England's mission is to protect and improve the nation's health and to address inequalities through working with national and local government, the NHS, industry and the voluntary and community sector. PHE is an operationally autonomous executive agency of the Department of Health.

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## Background

In June 2012 the Joint Committee on Immunisation and Vaccination (JCVI)<sup>1</sup> asked the Health Protection Agency, (now Public Health England) to undertake modelling studies to assess the impact and cost effectiveness of HPV vaccination of men who have sex with men (MSM), acknowledging this group are expected to receive very little indirect protection or benefit from the HPV vaccination programme, currently offered to adolescent females.

Since this time, JCVI has regularly reviewed all the available evidence on the disease epidemiology, vaccine efficacy and cost effectiveness of a HPV MSM immunisation programme in the UK.

On 7 October 2015, the JCVI considered its advice on the extension of HPV vaccination to MSM. They advised that a programme should be undertaken to vaccinate all MSM up to and including 45 years who attend GUM and HIV treatment services, subject to procurement of the vaccine and delivery of the programme at a cost-effective price

The Department of Health accepted this advice, and from June 2016, as part of a PHE-led pilot, the HPV vaccine will begin to be offered opportunistically to men who have sex with men (MSM) up to the age of 45, through existing appointments at selected local sexual health services.

This pilot will help evaluate whether an effective HPV programme for MSM can be delivered at a cost effective price across the country at a later date.

### What is HPV?

HPV is the abbreviation for the human papillomavirus. This is a double stranded DNA virus that infects the surface of the skin and mucosae of the upper respiratory and anogenital tracts.

There are over 100 types of HPV viruses of which about 40 infect the genital tract(1)

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<sup>1</sup> The Joint Committee on Vaccination and Immunisation (JCVI) is a statutory expert Standing Advisory Committee. Its purpose is to provide expert impartial advice to the Secretaries of State for Health for England, Scotland, Wales and Northern Ireland on matters relating to communicable diseases, preventable and potentially preventable through immunisation

The majority of HPV infections do not cause any symptoms and infection is usually cleared by the body's own immune system without the need for other treatment. However persistent infection with high risk HPV types such as types 16 and 18 can lead to cancer – most notably cancer of the anus, throat and penis, as well as cervical cancer in women. Other types of HPV such as 6 and 11 cause genital warts.

### Who does it affect?

HPV is one of the most common sexually transmitted infections in the UK. HPV infections are spread primarily by sexual contact with an infected partner, particularly through sexual intercourse but also by non-penetrative genital contact, including oral sex. Anyone who is sexually active can contract HPV. The risk of acquiring infection increases with the number of previous sexual partners, the introduction of a new sexual partner, and the sexual history of partners.

## HPV vaccination pilot for men who have sex with men (MSM) - vaccine eligibility

### What is the purpose of the programme?

The aim of the programme is to extend protection against HPV infection, HPV associated cancers and genital warts to the MSM population up to the age of 45 years through opportunistic vaccination at participating GUM and HIV clinics.

### Why MSM?

In all men 80-85% of anal cancers, 36% of oro-pharyngeal cancer and 50% of penile cancers are associated with HPV infection.(2,3) Men who have sex with men (MSM) bear a significantly increased burden of HPV related disease and adverse outcomes compared to heterosexual men. HPV type 16-associated anal cancers in particular are far more common in MSM compared to heterosexual men.(4,5)

Since September 2008 a national HPV Immunisation Programme for girls has been delivered throughout the UK to help prevent cervical cancer. The programme offers vaccination to school year 8 females (age 12-13 years) with a catch up for girls under 18 years of age. The girls' HPV vaccine programme has proved highly successful, with coverage exceeding 85% in the routine cohort. In addition to direct protection to females, the current HPV programme induces herd protection, which provides

substantial protection to heterosexual boys and men. However boys who become men who have sex with men will not benefit from this herd protection.

Following review of all the epidemiological and economic evidence as well as vaccine safety and efficacy, the JCVI consider a targeted HPV vaccination programme for MSM to be an effective way to reduce the number of preventable HPV infections in the MSM population and their onward transmission.

Why is the service being delivered through GUM and HIV clinics? MSM accessing GUM/HIV services are known to be at higher risk of HPV infection and disease. There is also more known about MSM using these services, which allowed the evidence for benefit from HPV vaccination to be assessed for this group of MSM. Sexual healthcare services are also the services where MSM are most likely to self-declare their sexual orientation.

Therefore, JCVI was able to consider delivering a targeted programme through GUM/HIV services and the best available evidence was found to show this to be a likely pragmatic and cost effective option at this time.

### Who is the vaccine recommended for?

The vaccine is recommended for all MSM up to and including 45 years of age, attending participating GUM or HIV clinics, regardless of risk, sexual behaviour or disease status.

### How will the programme be delivered?

A limited number of GUM and HIV clinics in all areas of England will be participating in the pilot.

During this pilot, participating clinics will be encouraged to systematically offer a full course of HPV vaccination to all MSM up to and including 45 years of age when they attend these services for existing appointments.

MSM will not be encouraged to actively seek vaccination during this phase of the pilot.

### Can the vaccine be offered to MSM who are older than 45 years?

Males older than 45 years are not eligible for HPV vaccination.

## What about other individuals with a similar risk profile?

JCVI considers that there may be considerable benefit in offering the HPV vaccine to other individuals who have a similar risk profile to that seen in the GUM attending MSM population, including some MSM over 45, sex workers, HIV+ve women, and HIV+ve men. Clinicians are able to offer vaccinations outside of the national programme using individual clinical judgement, and HPV vaccination could therefore be considered for such individuals on a case-by-case basis.

**Vaccine centrally procured for the HPV MSM programme however, should not be used for this purpose. In these instances, vaccine should be purchased directly from the manufacturer.**

## The vaccine

### What is the recommended vaccine for the programme and why?

Gardasil® is the recommended vaccine for the MSM vaccination programme and is the only market authorized quadrivalent HPV vaccine in the UK.

Gardasil® provides protection against four HPV strains: HPV-16 and HPV-18, the two high risk HPV types that can lead to cancer, and HPV-6 and HPV-11, the two HPV types that cause approximately 90 percent of all anogenital warts in males and females.

The vaccine is approved for use in females and males aged from 9 years of age.

### How does the vaccine work?

The vaccine is made from the proteins that make up the outer coat of the virus types. These proteins assemble into small spheres that are called virus-like particles (VLPs). VLPs are not infectious and cannot cause HPV-associated cancers or genital warts as they do not contain the virus's DNA. VLPs are however very immunogenic, which means that they induce high levels of antibody production by the body.

As with many other immunisations, when a person is vaccinated, their immune system mounts a response against these VLPs. When a person is then exposed to the live virus, the body's immune system reacts quickly to stop the infection.

## How effective is the vaccine?

Gardasil® has been shown to be highly effective in preventing the types of HPV infection for which it is indicated.

Prior infection with one HPV type does not diminish the efficacy of the vaccine against other HPV types included in the vaccine. To get the best protection, it is important the full course of vaccination is received.

In clinical trials in young women with no previous history of HPV infection, vaccine was 99% effective at preventing pre-cancerous lesions associated with HPV types 16 and 18.(6,7,8)

Gardasil® is also 99% effective at preventing genital warts associated with vaccine types in young women.(9)

A clinical trial of Gardasil® in men indicated that it can prevent anal cell changes caused by persistent infection, and genital warts.(10)

HPV vaccines have not been shown to have an impact on an existing infection or any of the outcomes of an existing HPV infection, such as anal genital warts but may boost immunity and prevent re-infection or reduce reoccurrences in people with established diseases. (11,12)

## How many doses of vaccine are required to ensure protection?

A course of 3 injections is needed for individuals aged 15 years of age and over. As part of the pilot, these 3 doses can be given over a period of up to 24 months. Recent studies indicate that for individuals under 15 years of age, a two dose course given a minimum of 6 months apart induces the same protection

## How long does protection last for?

Current studies suggest that protection is maintained for at least 10 years although protection is expected to last longer. Long term follow up studies are currently in place to evaluate this and will determine the need for any subsequent boosters.

## Are there any safety concerns about the HPV vaccine?

Gardasil® is a very safe vaccine. Its safety has been established through rigorous testing in clinical trials, followed by use of many millions of doses across the world over the past few years. As with any vaccine, some people may experience a side effect, but these are generally of short duration and are far outweighed by the expected benefits of the vaccine.

The UK Medicines and Healthcare products Regulatory Agency (MHRA) have published extensive reviews of HPV vaccine safety ([www.mhra.gov.uk/HPVvaccine](http://www.mhra.gov.uk/HPVvaccine))

The US health authorities have also posted very clear advice on their website supporting the safety of HPV vaccine

(<http://www.cdc.gov/vaccinesafety/Vaccines/HPV/index.html> )

Recently, concerns regarding the safety of the HPV vaccine have been raised in the UK and other European countries, with some parents and pressure groups linking the vaccination to a condition called Postural Orthostatic Tachycardia Syndrome (POTS). In June 2015, the JCVI concluded that it had no concerns about the safety of the HPV vaccine. The European Medicines Agency has also conducted an independent review and, in line with findings from the UK's Medicine and Healthcare Regulatory Agency (MHRA), concluded that available evidence does not support a causal link between the vaccine and the condition.

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2015/11/news\\_detail\\_002429.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/11/news_detail_002429.jsp&mid=WC0b01ac058004d5c1)

### How should the vaccine be stored?

Gardasil® should be stored in its original packaging between +2°C and +8°C (ideally aim for 5°C) and protected from light. Gardasil® should not be frozen.

Effectiveness cannot be guaranteed for vaccines unless they have been stored at the correct temperature. To ensure vaccines are ordered, stored and monitored as per national recommendations, healthcare professionals should familiarise themselves with Public Health England's Protocol for ordering, storing and handling of vaccines, available here:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/300304/Protocol\\_for\\_ordering\\_storing\\_and\\_handling\\_vaccines\\_March\\_2014.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/300304/Protocol_for_ordering_storing_and_handling_vaccines_March_2014.pdf)

Participating clinics should be aware there is a finite amount of vaccine available for the pilot. It is recommended healthcare professional order only what they need for a 2-4 week period rather than over-ordering or stockpiling vaccines.

## Vaccine administration

### How is the vaccine administered?

Gardasil® is administered by a single intramuscular injection into the upper arm (deltoid region). One dose has a volume of 0.5ml and the vaccine is provided in a pre-filled syringe.

Prior to use, the pre-filled syringe should be shaken well to obtain a white, cloudy suspension.

Two needles of different lengths are provided in the pack. Healthcare professionals should choose the appropriate needle to ensure an intramuscular (IM) administration depending on the vaccinee's size and weight.

A small air bubble may be visible in the prefilled syringe. This is not harmful and should not be removed prior to administration. This small bolus of air injected following administration of medication clears the needle and prevents a localised reaction from the vaccination. To try to expel it risks accidentally expelling some of the vaccine and therefore not giving the patient the full dose.

Healthcare professionals are encouraged to read the Summary of Product Characteristics (SPC) to ensure accurate constitution and delivery of the product.

### What is the dosing schedule?

#### **Individuals 15 years of age and older**

Gardasil® should be administered as a 3 dose schedule of 0.5 ml.

Due to the flexibility in the Gardasil® summary of product characteristics (SPC), variable spacing options for the three doses are possible. This should enable the administration of subsequent doses to be aligned with recommended GUM re-attendance in order to reduce introducing additional visits for vaccination only.

For guidance, in a 3 dose schedule, the second dose should be administered at least 1 month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should ideally be given within one year; however a 24 month period is clinically acceptable.

### ***Individuals under 15 years of age***

Gardasil® can be administered as a 2 dose schedule of 0.5ml given six months apart (0 and 6-24 months is clinically acceptable).

Any gap between doses of between 6 and 24 months is clinically acceptable. As long as the first dose was received before the age of 15 years the two dose schedule can be followed. For example, if first dose given aged 14 years but patient does not re-present in clinic until aged 17 years, only one further dose need be given.

**Why does the recommendation about the upper age limit for a two-dose schedule in adolescents differ from the information included in the Summary of Product Characteristics (SPC) for Gardasil®?**

In 2014 Gardasil® received licensing approval from the European Medicines Agency (EMA) for a two-dose schedule in adolescents. The two-dose schedule for Gardasil® is licensed for individuals aged nine up to and including 13 years of age. JCVI has agreed, however, to recommend a two-dose schedule up to (and including) 14 years of age for Gardasil®. The WHO's Strategic Advisory Group of Experts (SAGE) on immunisation also recently reviewed the evidence on HPV immunisation schedules. Upon review of the evidence, SAGE also recommended a two-dose schedule before the age of 15 years.

**What are the contraindications for receiving Gardasil®?**

There are very few individuals who cannot receive HPV vaccines. Where there is doubt, instead of withholding immunisation, appropriate advice should be sought from a consultant with immunisation expertise, a member of the screening and immunisation team or from the local health protection team.

Gardasil® should not be administered to those who have had:

1. A confirmed anaphylaxis to a previous dose of the vaccine OR
2. A confirmed anaphylaxis to any constituent or excipient of the vaccine

For the composition and full list of excipients of the vaccine, please refer to the manufacturer's Summary of Product Characteristics (SPC).

## What adverse reactions are commonly associated with the administration of Gardasil®?

In clinical vaccine trials, the most common adverse reaction observed were injection-site reactions (77.1% of vaccinees within 5 days following any vaccination visit). These include mild to moderate short-lasting pain at the injection site, immediate localised stinging sensation and redness at the injection site.

Other reactions commonly reported are headache, myalgia, fatigue, and low grade fever. These adverse reactions are usually mild or moderate in intensity.

For a detailed list of adverse reactions associated with Gardasil® please refer to the manufacturer's Summary of Product Characteristics (SPC) or the Patient Information Leaflet (PIL) that comes with each vaccine.

Any suspected side effects following administration should be reported to the Yellow Card Scheme <https://yellowcard.mhra.gov.uk/>

## Should HPV vaccine be administered to MSM in the eligible cohort with HIV infection?

Eligible MSM with human immunodeficiency virus (HIV) infection should be given HPV vaccine regardless of CD4 count, antiretroviral therapy use or viral load.

Evidence suggests individuals with HIV infection are at increased risk of acquiring HPV and persistent infection, as well as frequent carriage of multiple HPV types and increased risk of HPV related rapidly progressive malignancies.(13)

There are limited data on 3 dose schedules in HIV infected populations; however HPV vaccines are known to be safe and immunogenic when given to individuals infected with HIV with no adverse impact on CD4 cell counts or viral load observed.

There is no data to support giving fewer than 3 doses among HIV-infected individuals, therefore only a 3-dose schedule should be offered to individuals in the eligible cohort who are known to be HIV-infected. The immune response to this vaccination and its effectiveness may be less than that observed among those who are non-HIV infected.

## Can Gardasil® be given to individuals with an allergy to yeast?

Yes, yeast allergy is not a contraindication to the HPV vaccine. Even though Gardasil® is grown in yeast cells, the final vaccine product does not contain any yeast.(14)

### Does Gardasil® contain any preservatives such as thiomersal?

No, Gardasil® does not contain thiomersal. For a full list of excipients, (other substances contained in the vaccine besides the HPV antigens) healthcare professionals should read the manufacturer's Summary of Products Characteristics (SPC).

### Does Gardasil® contain any porcine gelatin?

No, Gardasil® does not contain porcine gelatin. For a full list of excipients (other substances contained in the vaccine besides the HPV antigens), healthcare professionals should read the manufacturer's Summary of Products Characteristics (SPC).

### Can Gardasil® be administered at the same time as other vaccines - for example Hepatitis B vaccine?

Yes, Gardasil® is an inactivated vaccine and will not be affected by, nor interfere with other inactivated or live vaccines given at the same time as or at any interval from each other.

Where two or more injections need to be administered at the same time, they should be given at separate sites, preferably in a different limb

If more than one injection is to be given in the same limb, they should be administered at least 2.5cm apart. The site at which each vaccine was given should be noted in the individual's health records.

### Should Hepatitis B vaccine be given to the same patients?

Yes, clinics/clinicians should take the opportunity to check (and correctly code) patients' hepatitis B virus (HBV) vaccination status. HBV vaccination uptake amongst MSM attending GUM clinics is below national targets, both for first dose uptake and for completion of three doses of vaccine(15).Recording of both HBV immunity and HBV vaccine delivery by clinician coding is also suboptimal. The UK's risk-based vaccination policy for HBV includes MSM and maintaining high vaccine coverage in MSM is important to avoid outbreaks of infection.

For useful links please see;

Public Health England. Immunisation against infectious diseases: Hepatitis B 18.  
<https://www.gov.uk/government/publications/human-papillomavirus-hpv-the-green-book-chapter-18a>

United Kingdom National Guideline on the Management of the Viral 1 Hepatitides A, B & C 2015

<http://www.bashh.org/documents/New%20Viral%20Hepatitides%20FINAL%20DRAFT%20MAY15.pdf>

### What happens if the vaccine course is interrupted or an individual misses a scheduled dose?

If the vaccine course is interrupted, it should be resumed but not repeated, ideally allowing the appropriate interval between the remaining doses. Individuals should be advised that although they will ultimately be protected if they receive the vaccine over a longer period of time they may remain susceptible to HPV infection prior to completing the course.

### What should I do if an individual following the 3 dose schedule has received their vaccine doses at less than the recommended interval?

Where vaccines have been given at less than the recommended interval, the dose should be repeated once the recommended time period has elapsed and at least four weeks from the last dose given. Patients should be advised this may lead to an increased risk of local reaction.

### What should I do if an individual following the 2 dose schedule has received their vaccine doses at less than a six month interval?

Two doses of Gardasil® given less than six months apart should not be considered adequate to provide long term protection and a third dose should be given according to the guidance on the 3 dose schedule above. See 'What is the dosing schedule?'

### What should I do if less than the recommended dose of vaccine is inadvertently administered?

In the event that Gardasil® vaccine is administered at less than the recommended 0.5 ml dose, the vaccination will need to be repeated because the dose that the individual received may not be sufficient to evoke a full immune response. Where possible, the dose should be repeated on the same day or as soon as possible after.

## Useful Links

Gardasil Summary of Product Characteristics. Available at the electronic Medicines Compendium (eMC) <https://www.medicines.org.uk/emc/medicine/19016>

Joint Committee on Vaccination and Immunisation

. <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-public-health-england/nhs-england-clinical-and-operational-guidance-for-the-hpv-for-msm-pilot>

Public Health England. Immunisation against infectious diseases: Human papillomavirus (HPV) 18a. <https://www.gov.uk/government/publications/human-papillomavirus-hpv-the-green-book-chapter-18a>

Public Health England. JCVI statement on HPV vaccination of men who have sex with men <https://www.gov.uk/government/publications/jcvi-statement-on-hpv-vaccination-of-men-who-have-sex-with-men>

Public Health England. Protocol for ordering, storing and handling vaccines. Available at:

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<http://www.bhiva.org/documents/Guidelines/Vaccination/2015-Vaccination-Guidelines.pdf>
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