

Human papillomavirus (HPV) immunisation programme

Factsheet for healthcare
professionals



Public Health
Agency

Background

In 2008, following advice received from the Joint Committee on Vaccination and Immunisation (JCVI), the HPV vaccine was introduced into the routine childhood immunisation programme in Northern Ireland and since has been offered routinely to all 12 to 13 year old females (school year 9). HPV vaccines protect against certain cancers caused by human papillomavirus (HPV) infection, including cervical cancer.

Around 1000 women die each year in the UK from cervical cancer. Having the HPV vaccine reduces the risk of getting cervical cancer by over 70%. The purpose of the immunisation programme is to reduce the burden of cervical cancer in the UK by protecting those who are at increased risk of disease.

What is HPV?

HPV is a double stranded DNA virus that infects the squamous epithelia including the skin and mucosae of the upper respiratory and anogenital tract. There are approximately 100 types of HPV of which about 40 infect the genital tract.

What diseases can HPV cause?

Although most infections are asymptomatic and self-limiting, genital infection by HPV is associated with genital warts and anogenital cancers in both men and women. In addition to cervical cancer, HPV is associated with less common cancers at other sites, including cancer of the vulva, vagina, penis and anus, and some cancers of the head and neck.

Genital HPVs are described as either:

- 'high-risk' types (also referred to as oncogenic) if they are associated with cervical cancer and the early changes in the cervix associated with cervical cancer. Or
- 'low-risk' types, if rarely or never found in cervical cancer, although some lead to the development of genital warts and may be associated with some other cancers.

Persistent infection by high-risk HPV types is detectable in more than 99% of cancers, of these high risks, HPV 16 is responsible for 60% and HPV 18 is responsible for 15% of all cervical

cancer types in Europe. A further 11 high risk types have been described. HPV types 6 and 11 cause the majority of cases of genital warts.

How is HPV infection spread?

Genital HPV infections are spread primarily by sexual contact, particularly through sexual intercourse but also by non-penetrative genital contact. Risk factors for acquiring HPV infection are related to sexual behaviour. Risk increases with number of new sexual partners, the sexual history of partners and the number of previous sexual partners.

Non-sexual routes of HPV transmission include transmission from mother to baby in the period immediately before and after birth, and hand to genital contact may explain some infections in childhood.

Will safe sex protect females better?

No. The use of condoms reduces but does not eliminate the risk of sexual transmission. HPV can spread by skin to skin contact and can be transmitted without penetrative sex.

Can HPV infection be treated?

Although HPV infection itself cannot be treated, the diseases it causes can often be treated quite successfully.

The HPV vaccine

What HPV vaccines are available?

The vaccines available protect against the two high-risk HPV types (16 and 18) that cause most cervical cancer and the two HPV types that cause the majority of genital warts (6 and 11). There are currently two different HPV vaccine products. Cervarix protects against two HPV types (16 and 18 – bivalent vaccine) and Gardasil protects against four HPV types (6, 11, 16 and 18 – quadrivalent vaccine). The two vaccine products are not routinely interchangeable and, ideally, one vaccine product should be used for the entire course.

Are the vaccines a live vaccine?

No, the vaccines are not live and they do not contain the HPV virus and therefore, cannot cause the HPV infection. The vaccines do not contain thimerosal or any other preservative. For a full list of excipients, healthcare professionals should read the manufacturer's Summary of Products Characteristics (SPCm).

How effective is the HPV vaccine in preventing cervical cancer?

HPV vaccines work extremely well. In England, among teenage females aged 16 to 18 years there has already been a significant decrease in the prevalence of the two main HPV types that can cause cervical cancer, with a 60% decrease in HPV 16 and a 73% in HPV 18. Scottish researchers have also shown a decline, probably due to cross-protection, in three other HPV types linked to cancer (types 31, 33 and 45). The number of precancerous lesions in the cervix has already fallen by over 50% since the programme began in Australia, Denmark and Scotland.

These vaccines do not protect against all HPV types that cause cervical cancer. However, there

is evidence of some protection against some of these types that are not in the vaccines (cross protection).

Who will receive the vaccine?

The vaccine is offered routinely to females aged 12 to 13 years (school year 9). Older females, under the age of 18 were offered the vaccine through a catch-up programme that began in September 2008. This programme has finished, but females aged less than 18 years who have not received the vaccine can still receive it free of charge if they ask their doctor.

What is the recommended vaccine for the programme?

The national immunisation programme began in 2008 using the Cervarix vaccine however, in 2012, the programme changed to use the Gardasil vaccine. In September 2014 the programme changed, from a three dose to a two dose schedule, provided vaccination is initiated prior to 15 years of age. A three dose schedule remains necessary if immunisation is initiated after the females' 15th birthday.

What is the current HPV vaccination schedule?

For females aged less than 15 years of age, the JCVI recommend a two dose schedule of 0, 6-24 months for both vaccines. For females commencing the course at age 15 years or above a three dose vaccination schedule of 0, 1, 4-6 months is appropriate for both vaccines. For females completing a three dose schedule, all three doses should ideally be given within a 12-month period. The female must complete the full two or three dose course to ensure they are fully protected.

Why has the vaccine changed?

Cervarix was chosen for the initial vaccine supply. When this was reviewed in 2011, Gardasil offered the best value and so was chosen for the next contract.

What if a female started the course with Cervaix but has not yet completed it?

There is no longer a supply of Cervarix available in the UK. For females who started the schedule with Cervarix, but did not complete the vaccination course, the course can be completed with Gardasil. The course should be completed according to a vaccination schedule of 0, 1, 4-6 months or 0, 6-24 months, depending on the age of the female when she received the first dose and whether one or two doses have already been given.

Why has the schedule changed from three to two doses?

In March 2014 the JCVI advised that based on the latest immunological evidence the efficacy and duration of protection in adolescents vaccinated using a two dose schedule administered as a prime and boost (separated by a minimum of six months) was likely to be the same as a three dose schedule, provided the first dose is received under 15 years of age.

Is there a cut off age for when you can start the two-dose schedule?

Yes. The two-dose schedule should only be started in females up to (and including) 14 years of age.

What if a female has not had her first HPV vaccine dose by the age of 15 years?

Females who have not had their first dose of HPV vaccine by the time they are 15 years old should be offered the three dose schedule. This is because the response in older females is not quite as good, so it has been agreed that they should be offered three doses at zero, one and six months.

What if a female has had the first two doses of the previous three dose schedule, does she still need the third one now?

This depends on the interval between the doses. Females who commenced a three dose schedule either before or after their fifteenth birthday and who have received two doses of vaccine less than six months apart should complete the three dose schedule as originally planned.

Females who commenced a three dose schedule before the age of 15 years and who received the first two doses of vaccine at least six months apart do not require a third dose and should be considered to have completed the full course.

What if a female receives two doses less than six months apart?

Two doses 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 dosage and schedule in the Green Book HPV chapter.

What happens if the two dose course is interrupted?

If the two dose course is interrupted, it should be resumed (using the same vaccine) but not repeated, even if more than 24 months have elapsed since the first dose and regardless of the age at which the female presents.

What if a female presents with incomplete immunisation status?

Where a female in the target cohort aged over 12 and less than 18 years presents with an incomplete vaccination history, every effort should be made to clarify what doses she has had and when she received them. A female who has started but did not complete the schedule before reaching the age of 18 years, should complete the vaccination course at the minimum interval where possible (see Green Book). If the course is interrupted then it should be resumed but not repeated.

How long does protection last for?

Efficacy studies have shown the vaccine to be effective for ten years, with no evidence of waning immunity. Data from clinical trials and ongoing research tell us that the protection provided by HPV vaccine will provide life time protection from these viruses because the immune system develops antibodies to the virus after the vaccination.

Do girls who have been vaccinated still need to attend for cervical screening?

Yes, it is very important that girls who have received the HPV vaccine still attend for cervical screening at the recommended age. The vaccine protects against seven out of 10 cervical cancers, so it is still important for girls to have regular smear tests when they are adults.

Vaccine safety

How do I know HPV vaccine is safe?

Vaccines undergo rigorous safety testing as part of the licensing process. The safety of HPV vaccines was tested in thousands of volunteers before the vaccines were approved. Subsequently, since the HPV vaccine was licensed in 2006 it has been strictly monitored and frequently reviewed by many national and international bodies including:

- the Medicines and Healthcare Products Regulatory Agency (MHRA)
- the European Medicines Agency (EMA)
- the Global Advisory Committee on Vaccine Safety of the World Health Organization; and
- the Centers for Disease Control and Prevention in the US.

All international bodies have continually reported that HPV vaccines are safe with no known long-term side effects. The only known severe reaction to the HPV vaccines is a severe allergic reaction which occurs in about 1 in every million girls who are given the vaccine.

In May 2016 the UK Medicines and Healthcare Regulatory Agency reported:

“More than three million girls have been vaccinated so far in the UK with HPV vaccine and tens of millions more have been vaccinated globally. As with all vaccines, safety remains under continual review, and HPV vaccine has a very good safety record”.

Are there any side effects with the vaccine?

Like any vaccine or medication, HPV vaccines can cause side effects. Some people have mild side effects after getting the HPV vaccine including, pain, swelling, or redness in the arm where the vaccine was given; fever, headache or feeling tired, nausea, vomiting or stomach pain or muscle and joint pain. Occasionally girls faint after receiving the vaccine and should be observed for approximately 15 minutes after vaccine administration.

A detailed list of adverse reactions associated with Cervarix® and Gardasil® is available in the Summary of Product Characteristics (SPC) and Patient Information Leaflet (PIL) for each vaccine, which can be accessed at the Medicines.org.uk website, <https://www.medicines.org.uk/emc/medicine/19016>. Suspected side effects should be reported to the Yellow Card Scheme www.mhra.gov.uk

Are side effects more frequently reported after HPV vaccination than for other vaccines?

No. To date, the number of reports to the MHRA of suspected side effects for HPV vaccines is not unusual. Over the past few years several studies based in different countries have found no evidence of a link between the HPV vaccine and a range of serious and chronic illnesses. Over 100 million people worldwide in countries like the United States, Canada, Australia and New Zealand have safely received the HPV vaccine. Not one of these people anywhere in the world has been medically proven to have had a long term side effect from getting the vaccine.

Concerns about complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS) following HPV vaccination have been raised in certain geographic locations. CRPS is a chronic pain syndrome affecting a limb, while POTS is a condition where the heart rate increases abnormally on sitting or standing up, together with symptoms such as dizziness, fainting and weakness, as well as headache, aches and pains, nausea and fatigue. In some patients they can severely affect the quality of life. Both syndromes have been known for many years, before the vaccine was introduced and are relatively common in young adolescents. Available estimates suggest that in the general population around 150 girls/young women per million aged 10 to 19 years may develop CRPS each year, and at least 150 girls and young women per million may develop POTS each year.

In November 2015 the European Medicines Agency completed its review of the evidence surrounding reports of both syndromes, in girls/young women that had received HPV vaccines. The review concluded that the occurrence of CRPS and POTS in vaccinated girls was no higher than would be expected in girls in the general

population and that there is no evidence the vaccines can trigger these syndromes. Overall, ecological analyses suggested that there had been no change in the incidence of these syndromes in girls aged 12-20 years after the introduction of the vaccination despite high uptake.

What are the contraindications for receiving HPV?

There are very few individuals who cannot receive HPV vaccine. The vaccine should not be given to those who have had a confirmed anaphylactic reaction to a previous dose of HPV vaccine, or a confirmed anaphylactic reaction to any components of the vaccine. **Pregnant women should not receive the vaccine.** If an individual is acutely unwell, immunisation may be postponed until they have fully recovered.

Should a female receive the vaccine if she is pregnant or breastfeeding?

HPV vaccine is not recommended in pregnancy. This is not because of any specific safety concerns with giving the HPV vaccine during pregnancy but due to limited information on using the vaccine in pregnant women. However, if a female is pregnant, they should be offered the vaccine as soon as possible after pregnancy. If a woman finds out she is pregnant after she has started a course of HPV vaccine, she should complete her pregnancy before finishing the appropriate schedule. Routine questioning about last menstrual period and/or pregnancy testing is not required prior to HPV vaccination.

There are no specific safety concerns with a female receiving the Gardasil vaccine when she is breastfeeding. However, the effect on breastfed infants following the administration of Cervarix to their mothers has not been evaluated in clinical studies. Therefore, Cervarix should only be used during breastfeeding when the possible advantages outweigh the possible risks.

What should happen if the HPV vaccine is inadvertently administered to a pregnant woman?

For women, who were inadvertently immunised whilst pregnant or shortly before becoming pregnant, no specific safety concerns have been identified in either the outcome of pregnancy or foetal development. However, if a woman finds out she is pregnant after she has started a course of HPV vaccine, she should discuss this with her GP who can then report this to the Public Health England (PHE) register directly by visiting this website: <https://www.gov.uk/guidance/vaccination-in-pregnancy-vip>

What if a female is immunosuppressed or is known to be HIV infected?

There is no data for two dose schedules for immunocompromised individuals. Therefore a **three** dose schedule should be used for females known to be HIV infected, including those on antiretroviral Rx, or known to be immunocompromised at the time of immunisation. Re-immunisation should be considered after completion of treatment or recovery. Specialist advice should be sought.

Vaccine eligibility for the routine HPV immunisation programme

Why is the national programme being routinely offered to females aged 12-13 years?

The vaccine has been shown to induce a better immune response in young females between 9 and 15 years of age compared with older teenage females and young women (aged 16–26 years). The vaccine will protect the females before adulthood and the likely exposure to HPV.

Should females wait and get the vaccine when they are older?

No. Before the vaccination programme, over 70% of women caught HPV infection, and rates increased rapidly after 15 years of age. Vaccination of younger females is more effective and offers protection prior to possible exposure to the virus. If however, a female does not receive the vaccine at the routine age they are still eligible and should be offered the vaccine if they are less than 18 years old. Prior infection with one type of HPV does not mean that the vaccine will not offer protection against other types of HPV.

Can females aged 18 or over who had previously been eligible for the vaccine still receive it?

Vaccination for females over the age of 18 years is not covered by the national HPV vaccination programme. However, for females who commenced, but did not complete the vaccination course, it is reasonable to complete their HPV vaccination course after the age of 18 years (see page 4).

Are older females still at risk of contracting HPV?

All women who are sexually active are at risk of HPV infection. Risk of a new HPV infection decreases quite markedly for most women over the age of 25 years, by this time many women will already have become infected and/or change sexual partners less frequently. For sexually active older women who are already likely to have been infected by HPV, participation in the Cervical Screening Programme (to detect disease caused by existing infection) remains the best way to protect themselves against cervical cancer.

Can males contract HPV?

Yes males who are sexually active are at risk of contracting HPV. HPV infection can increase a man's risk of getting genital cancers, although these cancers are not common. HPV can also cause genital warts in men, just as in women.

Will males receive the vaccine?

As males do not suffer from cervical cancer, the benefits of HPV vaccination are different and less clear for males than for females, and vaccination

of males has not been found to be cost-effective in the UK. The protection against genital warts offered by Gardasil has been clearly shown for both males and females. Males will receive cross protection from females being vaccinated. Men who have sex with men (MSM) in Northern Ireland will be eligible to receive the HPV (Human Papilloma Virus) vaccine as they will not benefit from the herd effect of vaccinating women. This is a targeted vaccination programme for MSM aged up to 45 who attend GUM and HIV clinics.

Vaccine delivery and administration

How will the programme be delivered?

The vaccine is given through a school based programme in Year 9, to ensure high vaccine uptake. The school health team will let the female know the date the school immunisation team will attend the school to give the HPV vaccine. If a female misses the vaccine in school she will be offered a further opportunity to receive the vaccine in year 10.

How is HPV administered and where is it administered?

The vaccine will usually be given in the upper arm by intramuscular injection. However, for individuals who have a bleeding disorder, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

Can the vaccine be administered at the same time as other vaccines?

HPV vaccines can be given at the same time as other vaccines such as Td/ IPV, MMR, Influenza,

MenC and hepatitis B. If multiple vaccines are to be administered, they should be given at a separate site, preferably in a different limb. If given in the same limb, they should be given at least 2.5cm apart. The site at which each vaccine was given should be noted in the individual's records.

What should I do if the vaccine was administered at less than the recommended dose?

In the event that the vaccine is administered at less than the recommended dose, vaccination will need to be repeated because the dose that the female received may not be sufficient to evoke a full immune response. Where possible, the dose of vaccine should be repeated on the same day or as soon as possible after. In the event that the additional dose of vaccine cannot be administered at the same visit or day, arrangements should be made to administer the additional dose as soon as possible, thus not to delay future doses.

Useful links

NHS choices

<http://www.nhs.uk/conditions/vaccinations/pages/hpv-human-papillomavirus-vaccine.aspx>

The human papillomavirus vaccine: beating cervical cancer – the facts

<https://www.gov.uk/government/publications/the-human-papillomavirus-vaccine-beating-cervical-cancer-the-facts>

Jo's Trust

<https://www.jostrust.org.uk/about-cervical-cancer>

Human Papillomavirus (HPV) Vaccine Information

<http://www.hse.ie/eng/health/Immunisation/pubinfo/schoolprog/HPV/>

Human Papillomavirus (HPV)

<https://www.cdc.gov/hpv/index.html>

European Medicines Agency

www.ema.europa.eu/

The Green Book

<https://www.gov.uk/government/publications/human-papillomavirus-hpv-the-green-book-chapter-18a>
Vaccination of individuals with uncertain or incomplete immunisation status. Public Health England.
Updated 20 June 2016.

References

- Centres for Disease and Control Prevention, 2017. Human Papillomavirus (HPV). [Internet] Accessed 20 March 2017. Available at: <https://www.cdc.gov/hpv/index.html>
- European Medicines Agency, 2016. HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/HPV_vaccines_20/European_Commission_final_decision/WC500196773.pdf [Internet] Accessed 14 March 2017.
- Health Service Executive National Immunisation Office, 2017. Human Papillomavirus (HPV) Vaccine Information. Available at: <http://www.hse.ie/eng/health/Immunisation/hcpinfo/OtherVaccines/hpv/giveadvicehpv.html> [Internet] Accessed 16 March 2017.
- Medicines and Healthcare products Regulatory Agency, 2016. Human papillomavirus (HPV) immunisation programme. Available at: https://www.gov.uk/search?q=hpv&show_organisations_filter=true [Internet] Accessed 14 March 2017.
- Pollock, K.G.J.et al. 2014. Reduction of low- and high-grade cervical abnormalities associated with high uptake of the HPV bivalent vaccine in Scotland. British Journal of Cancer. 111, pp.1824–1830
- Public Health England, 2014. Beating cervical cancer – the facts. The human papillomavirus vaccine The virus, the diseases and the HPV vaccine. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/345955/8874-HPV-the-Facts-05.pdf [Internet] Accessed 22 March 2017.
- Public Health England, 2016. Factsheet for Healthcare Professionals. Human papillomavirus (HPV) vaccination and Cervical Cancer addressing the myths. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/580513/PHE_HPV_School_Nurse_A4_factsheet_1.pdf [Internet] Accessed 16 March 2017.
- Vichnin, M. et al. 2015. An Overview of Quadrivalent Human Papillomavirus Vaccine Safety: 2006 to 2015. Paediatric Infectious Disease Journal. 34(99), pp.983-91
- World Health Organisation, 2016. Human Papillomavirus (HPV) and Cervical Cancer. Available at: <http://www.who.int/mediacentre/factsheets/fs380/en/> [Internet] Accessed 16 March 2017.