Patient leaflet in accordance with
the Pharmacists' Regulations (Preparations) – 1986
The medicine is dispensed
according to a physician's prescription only

Cervarix™, Suspension for intramuscular injection

0.5 ml suspension of Human Papillomavirus vaccine contains:
HPV type 16 L1 20 mcg
HPV type 18 L1 20 mcg
List of the ingredients detailed in section 6.

Read the entire leaflet carefully before using the vaccine. This leaflet contains concise information about the vaccine. If you have any other questions, refer to the physician or the pharmacist.

This vaccine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. What is the vaccine intended for?

Cervarix is a vaccine for use in females from the age of 9 years for the prevention of premalignant genital (cervical, vulvar and vaginal) lesions and cervical cancer causally related to certain oncogenic Human Papillomavirus (HPV) types.

Therapeutic group: Papillomavirus vaccines.

The Human Papillomavirus (HPV) types contained in the vaccine (HPV types 16 and 18) are responsible for approximately 70% of cervical cancer cases and 70% of HPV-related pre-cancerous lesions of the vulva and vagina. Other HPV types can also cause cervical cancer. Cervarix does not protect against all HPV types.

When a female is vaccinated with Cervarix, the immune system (the body's natural defence system) will make antibodies against HPV types 16 and 18. In clinical trials Cervarix has been shown to prevent HPV related diseases in females aged 15 years and older. Cervarix also stimulates production of antibodies in females 9-14 years of age.

Cervarix is not infectious and so, it cannot cause HPV related diseases.

Cervarix is not used to treat HPV related diseases already present at the time of vaccination.

2. Before using the vaccine

Cervarix should not be given:

- if you are sensitive (allergic) to any of the active substances or any of the additional ingredients of this vaccine (listed in section 6). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if you have a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to the physician first.

Special warnings regarding the use of the vaccine

Before the treatment with Cervarix, tell the physician or the pharmacist:

- if you have a bleeding problem or bruise easily.
- if you have any disease which reduces your resistance to infection such as HIV infection.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore, tell the physician or nurse if you or your child fainted with a previous injection.

As with all vaccines, Cervarix may not fully protect all people who are vaccinated.

Cervarix does not protect people from diseases caused by infection with HPV types 16 or 18 if they are already infected with Human Papillomavirus type 16 or 18 at the time of vaccination.

Although vaccination may protect you against cervical cancer, it is not a substitute for regular cervical screening. You should continue to follow your physician's advice on cervical smear/Pap test (test to screen for changes in cells of the cervix caused by an HPV infection) and preventative and protective measures.

As Cervarix will not protect against all types of Human Papillomavirus, appropriate precautions against exposure to HPV and sexually transmitted diseases should continue to be used.

Cervarix will not protect against other diseases that are not caused by Human Papillomavirus.

Other medicines and Cervarix

If you are taking, have recently taken or might take any other medicines including, non-prescription medicines and food supplements or have recently received any other vaccine, tell the physician or the pharmacist.

Cervarix can be given with a combined booster vaccine containing diphtheria (d), tetanus (T) and pertussis [acellular] (pa) with or without inactivated poliomyelitis (IPV), (dTpa, dTpa-IPV vaccines), or with a combined hepatitis A and hepatitis B vaccine or a hepatitis B vaccine, at a separate injection site (another part of your body, e.g. the other arm) during the same visit.

Cervarix may not have an optimal effect if used with medicines that suppress the immune system.

In clinical trials, oral contraceptives (e.g. the pill) did not reduce the protection obtained by Cervarix.

Pregnancy and breast-feeding

There are insufficient data concerning the use of Cervarix during pregnancy. If pregnancy occurs during the course of vaccination your physician should be consulted. It is recommended to postpone vaccination until after completion of the pregnancy.

If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your physician for advice before you are given this vaccine.

Driving and using machines

Cervarix is not likely to affect your ability to drive or operate machines. However, do not drive or operate any machines if you are feeling unwell.

3. How should you use the vaccine?

The dosage and treatment will be determined only by the physician.

How the vaccine is given

The physician or nurse will give Cervarix as an injection into the muscle of the upper part of the arm.

The usual dosage is:

Cervarix is intended for females from 9 years of age onwards.

The total number of injections you will receive depends on your age at the time of the first injection:

If you are between 9 and 14 years old, Cervarix can be administered by your physician according to the following 2-dose schedule:

First injection: at chosen date
Second injection: 6 months after first injection

If you are 15 years old or above, Cervarix can only be administered by your physician according to the following 3-dose schedule:

First injection: at chosen date
Second injection: 1 month after first injection
Third injection: 6 months after first injection

When Cervarix is given for the first dose, it is recommended that Cervarix (and not another vaccine against HPV) be given for the complete vaccination course.

The vaccine should never be given into a vein.

Cervarix is not recommended for vaccinating girls below 9 years of age.

If you miss a dose

It is important that you follow the instructions of your physician or nurse regarding return visits. If you forget to go back to your physician at the scheduled time, ask your physician for advice.

If you do not finish the complete vaccination course (two or three injections depending on your age at vaccination), you may not get the best response and protection from the vaccination.

4. Side effects

As with any medicine, use of Cervarix may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Side effects that occurred during clinical trials with Cervarix were as follows:

♦ Very common (side effects which may occur in more than 1 per 10 doses of vaccine):
- pain or discomfort at the injection site
- redness or swelling at the injection site
- headache
- aching muscles, muscle tenderness or weakness (not caused by exercise)
- tiredness.

♦ Common (side effects which may occur in less than 1 per 10 but more than 1 per 100 doses of vaccine):
- gastrointestinal symptoms including nausea, vomiting, diarrhoea and abdominal pain
- itching, red skin rash, hives (urticaria)
- joint pain
- fever (≥38°C).

♦ Uncommon (side effects which may occur in less than 1 per 100 but more than 1 per 1,000 doses of vaccine):
- upper respiratory tract infection (infection of the nose, throat or trachea)
- dizziness
- other injection site reactions such as hard lump, tingling or numbness.

Side effects that have been reported during marketed use of Cervarix include:

- allergic reactions. These can be recognised by:
  itchy rash of the hands and feet,
  swelling of the eyes and face,
  difficulty in breathing or swallowing,
  sudden drop in blood pressure and loss of consciousness.
  These reactions will usually occur before leaving the clinic. However, if your child gets any of these symptoms you should contact a physician urgently.
- swollen glands in the neck, armpit or groin
- fainting sometimes accompanied by shaking or stiffness.

5. How to store the vaccine?

- Avoid poisoning! This vaccine and any other vaccine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the vaccine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C – 8°C). Do not freeze.
- Store in the original package in order to protect from light.

6. Additional information

What Cervarix contains

- The active substances are:

Human Papillomavirus[1] type 16 L1 protein[2,3,4]	20 micrograms
Human Papillomavirus[1] type 18 L1 protein[2,3,4]	20 micrograms

[1]Human Papillomavirus = HPV
[2]adjuvanted by AS04 containing:

3-*O*-desacyl-4'- monophosphoryl lipid A (MPL)[3]	50 micrograms
[3]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$)	0.5 milligrams Al^{3+} in total

[4]L1 protein in the form of non-infectious virus-like particles (VLPs) produced by recombinant DNA technology using a Baculovirus expression system which uses Hi-5 Rix4446 cells derived from the insect *Trichoplusia ni.*

- The other ingredients are:
  sodium chloride (NaCl), sodium dihydrogen phosphate dihydrate ($NaH_2PO_4.2\ H_2O$) and water for injections.

What does the vaccine look like and what is the content of the package

Cervarix is a turbid white suspension.

Cervarix is available in vials for 1 dose (0.5 ml) in packs of 1, 10 and 100.

Cervarix is available in pre-filled syringes (0.5 ml) with or without needles in packs of 1 and 10.

Not all pack sizes may be marketed.

- License Holder and address: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer and address: GlaxoSmithKline Biologicals S.A., Rixensart, Belgium.
- This leaflet was checked and approved by the Ministry of Health in: August 2014.
- Registration number of the vaccine in the National Drug Registry of the Ministry of Health: 138-09-31676

The following information is intended for healthcare professionals only:

Cervarix should be administered as soon as possible after being removed from the refrigerator. However, the stability has been demonstrated when stored outside the refrigerator for up to 3 days at temperatures between 8°C and 25°C or for up to 1 day at temperatures between 25°C and 37°C.

A fine white deposit with a clear colourless supernatant may be observed upon storage. This does not constitute a sign of deterioration.

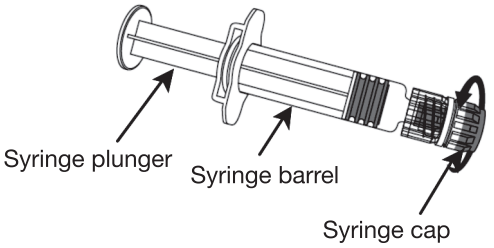
The content of the vial or syringe should be inspected visually both before and after shaking for any foreign particulate matter and/or abnormal physical appearance prior to administration.

In the event of either being observed, discard the vaccine.

The vaccine should be well shaken before use.

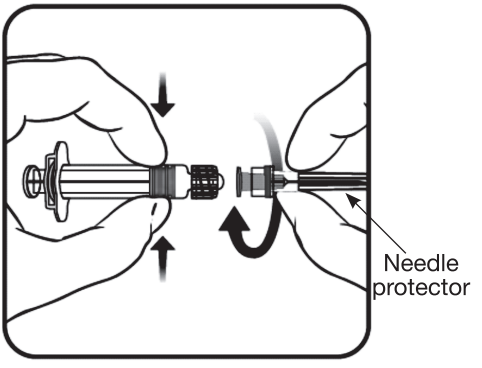
Instructions for administration of the vaccine presented in pre-filled syringe

1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.



2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock.

3. Remove the needle protector, which on occasion can be a little stiff.



4. Administer the vaccine.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.