

To those who wish to receive Uterine head cancer vaccination (Cervarix)

To children and guardians

**~this is essential information, please make sure you read it~
If the first dose of Cervarix is administered, the second and third doses should be administered with Cervarix.**

The efficacy and safety of other HPV vaccines in the second and third doses has not been confirmed.

[1] Uterine Head Cancer and Carcinogenic Human Papillomavirus (HPV)

- (1) Cervical cancer is a cancer of the cervix (the entrance to the uterus) that occurs rapidly in women in their 20s and 30s. Cervical cancer often goes undetected because there are almost no subjective symptoms in the early stages of the disease. In the early stages of the disease, there are few subjective symptoms, so detection of the disease is often delayed. As the cancer progresses, there may be irregular bleeding or bleeding during intercourse.
- (2) Cervical cancer is a disease caused by infection with a virus called carcinogenic HPV.
- (3) In many cases, carcinogenic HPV infection is temporary and the virus is eliminated spontaneously, but if the infection continues for a long time, cervical cancer may develop.
- (4) Carcinogenic HPV is a common virus that infects many women, not just special people.
- (5) There are about 15 types of oncogenic HPV, among which HPV types 16 and 18 are the most common types found in cervical cancer. These two types of carcinogenic HPV are found in 67% of Japanese cervical cancer patients.

[2] There is a vaccine that prevents infection with carcinogenic HPV types 16 and 18.

- (1) Cervarix does not prevent infection with all carcinogenic HPV types, but it does prevent infection with two types of carcinogenic HPV, HPV type 16 and HPV type 18, which are often found in cervical cancer.

(2) Cervarix **does not eliminate the virus, slow down the progression of cervical cancer or precancerous lesions (abnormal cells before they become cancerous), or treat patients who are infected with carcinogenic HPV at the time of vaccination.**

(3) As mentioned above, it cannot protect a person infected with both HPV 16 and HPV 18 at the same time but it is rare to be infected both HPV16 and HPV18. However, a person infected with HPV 16 can be expected to be protected against HPV 18 and a person infected with HPV 18 can be also protected against HPV 16. Cervarix" has not been reported to worsen symptoms in people infected with carcinogenic HPV.

[3] The vaccine is effective if given before infection with carcinogenic HPV types 16 and 18.

(1) Cervical cancer is most common in women in their 20s or later, but it takes several years to a decade to develop cervical cancer after infection with carcinogenic HPV.

(2) Vaccinating against cervical cancer in your early teens, when the chance of contracting carcinogenic HPV is low, can more effectively prevent the onset of cervical cancer.

(3) Even after the vaccination, not all lesions caused by carcinogenic HPV can be prevented, so it is necessary to undergo cervical cancer screening for early detection. The public cervical cancer screening conducted by municipalities is for people over 20 years of age, and is conducted at intervals of once in a year or two. Even if you were vaccinated in your teens, you should undergo regular cervical cancer screening after the age of 20. There is no public screening system for teenagers. If you have any concerns, please consult the medical institution where you received the vaccine immediately.

[4] Please do not receive the vaccine if you have any of the following conditions

1) Those with obvious fever (usually over 37.5 °C).

(2) Those who are suffering from serious acute illness.

(3) Those who have experienced hypersensitivity reactions (including severe allergic reactions such as breathing difficulties and generalized hives that usually appear within 30 minutes after inoculation) to the ingredients of Cervarix (please ask your doctor for details).

4) Other people who have been told by their physician that they should not receive vaccinations.

[5] Please consult your doctor before vaccination if you are one of the following

1) Those with low platelets or those who bleed easily.

(2) Those who have an underlying disease such as heart disease, kidney disease, liver disease, blood disease, or developmental disorder.

(3) Those who have had a fever within 2 days after vaccination in the past.

(4) Those who have had convulsions in the past.

(5) Those who have been diagnosed with abnormal immune status in the past, or those who have a close relative with congenital immunodeficiency.

6) Pregnant women or those who may be pregnant (including during the 3 times of vaccination).

(7) Those who are currently breastfeeding.

[6] Cervarix and its effects

(1) Cervarix is for females 10 years and older.

(2) Cervarix has been shown to be effective in preventing HPV type 16 and 18 infections and precancerous lesions in women aged 15 to 25 years through clinical trials. There is no data on the preventive effect in girls aged 10~14 years and women aged 26 years and older, but it has been confirmed that antibodies are produced in the same way as in women aged 15~25 years.

(3) As for how long the preventive effect of Cervarix will last.

it has been confirmed that in adult females, antibodies from Cervarix vaccination last for 9.4 years, and the preventive effect against precancerous lesions lasts for up to 9.4 years (average of about 8.9

years) (overseas clinical trial results). The duration of antibodies and efficacy is still under observation, and is expected to be further extended in the future. The amount of antibody needed to prevent the development of cervical cancer is not known at this time. It is possible that additional Cervarix vaccinations may be required in the future, so please pay attention for further information.

(4) Cervical cancer is often thought to develop after persistent infection with carcinogenic HPV or precancerous lesions, and prevention of these can prevent cervical cancer. It takes several years to a decade after infection with carcinogenic HPV for cervical cancer to develop. Clinical trials have confirmed that Cervarix can prevent persistent infection with carcinogenic HPV and precancerous lesions, but the preventive effect on cervical cancer has not been confirmed and is still being investigated overseas. Further information will be available on our website as it becomes available.

[7] In order to obtain sufficient prophylactic effect of Cervarix, three doses of vaccination are required.

(1) Three inoculations are required to obtain sufficient preventive effect.

(2) The vaccine is injected into the muscle of the arm.

(3) If you become pregnant in the middle of the 3 times of vaccination, you cannot continue the vaccination. Please consult your doctor about subsequent inoculations.

[8] Symptoms after inoculation

(1) Two types of adjuvants (immune-supporting ingredients) are added to " Cervarix " in order to maintain the full efficacy of the vaccine for a long time, one is aluminum salt (commonly used in vaccines sold in Japan) and the other is MPL (deacylated-4'-monophosphoryl lipid A), both of them are also used in new vaccines recently introduced overseas.

(2) After inoculation with Cervarix, the injection site may become swollen or painful.

(3) The pain and swelling in the injected area is caused by the same

mechanism that protects against viral infection in the body. It usually goes away in a few days.

(4) More than 7 million people overseas and 3.4 million people in Japan have been inoculated with Cervarix (based on estimates as of February 2011). In clinical trials overseas, about 90,000 people have been inoculated.

[9] The most common adverse reactions to Cervarix

(1) The main adverse reactions considered to be related to inoculation have been reported as follows.

- Frequency Over 10%: Itching, pain, redness, and swelling at the injection site, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain, etc.), muscle pain, joint pain, headache, and fatigue.
- Frequency 1-10%: Rash, hives, lumps at the injection site, dizziness, fever, upper respiratory tract infection
- Frequency 0.1-1%: Tingling/mushy sensation at the injection site, numbness, generalized weakness
- Frequency unknown: Pain in the extremities, fainting, vasovagal reaction (lightheadedness, cold sweat, hypotension, chills, indisposition, ear sobs, slow pulse, rapid pulse), elevated AST (GOT) and ALT (GPT), uveitis, keratitis, and lymphadenopathy. In rare cases, anaphylaxis-like symptoms (angioedema, hives, dyspnea, etc.) may occur as a serious adverse reaction.

(2) In rare cases, anaphylaxis-like symptoms (angioedema, urticaria, dyspnea, etc.) may occur.

(3) Pay attention to your symptoms for one week after the vaccination. Consult your doctor if you have any worrisome symptoms such as severe pain or long-lasting pain.

(4) About the relief system based on the Pharmaceutical and Medical Devices Agency Law

If an adverse reaction occurs despite the proper use of Cervarix, resulting in illness or disability that requires hospitalization, the patient will be eligible for damage relief based on the Pharmaceuticals and Medical Devices Agency Law. Depending on the nature and extent of the health damage, after deliberation by the Pharmaceutical Affairs and Food Sanitation Council, medical

expenses, medical allowances, disability pension, survivor's pension, and survivor's lump-sum payment will be provided. If you experience any symptoms that concern you, please consult your doctor.

[10] Cautions after inoculation

- (1) Severe allergic symptoms and fainting as a vasovagal reflex may occur after inoculation, so please do not go home immediately after inoculation, but sit and watch for about 30 minutes.
- (2) After inoculation, hold the inoculation site lightly and do not rub it.
- (3) Keep the vaccination site clean after vaccination.
- (4) Refrain from excessive exercise on the day of vaccination.
- (5) Bathing on the day of vaccination is not a problem.

- **It has been confirmed that three doses of Cervarix are effective in preventing the disease.**
- **Even after the vaccination, please have regular cervical cancer checkups after the age of 20.**

Inoculation schedule	Month	Date	Time	Hour	Minute
Inoculation Institute					