SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medical Product

Papilovax

Suspension for injection in Prefilled Syringe, 0.5 ml

Human Papillomavirus vaccine (rDNA)

2. Qualitative and quantitative composition

Each 0.5 ml contains Human Papillomavirus Vaccine (rDNA) BP consisting of recombinant human papillomavirus type 16 L1 protein 40 µg and recombinant human papillomavirus type 18 L1 protein 20 µg.

Papilovax is a mixture of two-aluminum hydroxide adjuvant-absorbed recombinant L1 capsid proteins of human papillomavirus (HPV) type-16 and type-18 each self-assembled into virus-like particles (VLPs). The HPV-16 and HPV-18 L1 antigens are expressed in *Escherichia coli* by recombinant DNA technology. Excipients: Aluminum Hydroxide, Sodium dihydrogen phosphate, Disodium hydrogen phosphate, Sodium chloride, Polysorbate 80 & Water for injection

3. Pharmaceutical form

Suspension for injection. Turbid white suspension

4. Clinical Particulars

4.1 Therapeutic indications

Papilovax is indicated for women aged 9-45 years. It is used for preventing the following diseases caused by oncogenic human papillomavirus (HPV) types 16 and/or 18-

- Cervical cancer
- Cervical intraepithelial neoplasia Grade 2 or 3 (CIN2/3) and adenocarcinoma in-situ (AIS)
- Cervical intraepithelial neoplasia Grade 1 (CIN1) and persistent infections of HPV types 16 and/or 18

The risk of exposure to HPV increases with age, especially with sexual debut. Therefore, it is recommended to vaccinate as early as possible. It would be more beneficial to receive the vaccine at the earlier time between ages 9-45 years.

4.2 Posology and method of administration

4.2.1 Posology

The vaccination schedule depends on the age of the subject

Age at the time of the first injection	Age at the time of the first injection
9 to and including 14 years*	Two doses each of 0.5 ml. The second dose given between 5 and 13 months after the first dose
From 15 years and above	Three doses each of 0.5 ml at 0, 1, 6 months**

*If the second vaccine dose is administered before the 5th month after the first dose, a third dose should always be administered.

**If flexibility in the vaccination schedule is necessary, the second dose can be administered between 1 month and 2.5 months after the first dose and the third dose between 5 and 12 months after the first dose.

The need for a booster dose has not been established (see section 5.1). It is recommended that subjects who receive a first dose of Papilovax complete the vaccination course with Papilovax (see section 4.4). Paediatric population (children < 9 years of age) Papilovax is not recommended for use in children below 9 years of age due to limited data on safety and immunogenicity in this age-group.

4.2.2 Method of administration

- Papilovax is for intramuscular injection in the deltoid region (see also sections 4.4 and 4.5).
- Papilovax should under no circumstances be administered intravascularly or intradermally.
- No data are available on subcutaneous administration of Papilovax (see section 4.4).
- If Papilovax is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites (see section 4.5).
- The risk of exposure to HPV increases with age, especially with sexual debut. Therefore, it is recommended to vaccinate as early as possible. It would be more beneficial to receive the vaccine at the earlier time between ages 9-45 years.

4.3 Contraindication

- Hypersensitivity to the active substances or to any component of the excipients of vaccine.
- Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of this vaccine.

4.4 Special warnings and precautions for use

- Vaccination cannot replace the routine cervical cancer screening or other measures to prevent HPV infection and sexually transmitted diseases. Therefore, routine cervical cancer screening remains extremely important as recommended by the relevant health administrative departments.
- Prior to the vaccination, medical personnel should inquire and review the vaccinee's medical history (especially the prior vaccination history and any prior adverse reaction related to vaccination), and conduct clinical examination to evaluate the benefits and risks of vaccination.
- It is not recommended for populations other than those described in of the package insert.

- Like other vaccines for injection, appropriate medical emergency measures and monitoring methods should be prepared to ensure that those who develop allergic reactions after the injection
- Syncope (fainting) may occur after any dose of vaccine, leading to falls and injuries, especially in adolescents and young adults. Therefore, it is recommended that the observation on site be conducted for at least 30 minutes after each injection as required in the vaccination procedures.
- It has been reported that syncope associated with tonic-clonic seizures and other epileptiform seizures may occur after the vaccination with similar products overseas. Syncope associated with tonic-clonic seizures is usually transient, and it can be resolved spontaneously when the vaccinee is placed in a supine or head-down position and the cerebral perfusion is restored. Some vaccinees may experience psychogenic reactions before/after the vaccination, and measures should be taken to avoid injury from the syncope.
- Like other vaccines, the vaccination should be postponed in vaccinees with acute serious febrile illness. In case of current or recent fever symptoms, whether to postpone the vaccination depends mainly on the severity of the symptoms and their etiology. Low-grade fever and mild upper respiratory tract infection are not absolute contraindications to vaccination.
- The vaccine should be used with caution in vaccinees with thrombocytopenia or any coagulation disorder.
- Like any other vaccine, vaccination with HPV vaccine may not ensure the protective effect for all vaccinees.
- It is only used for preventive purposes, but not indicated for the treatment of existing HPV-related lesions or preventing the progression of lesions.
- It cannot prevent lesions caused by all high-risk types HPV infections. It has not been proved that it can prevent the lesions caused by the infection of non-vaccine types of HPV as well as the diseases not caused by HPV infection.

There has been no data on the use of HPV vaccine in vaccinees with impaired immune system (such as receiving the medication of immunosuppressive agents). Like other vaccines, vaccination in immunocompromised people

4.5 Interaction with other medical products and forms of interaction

- There are no data to assess the concomitant use of HPV vaccine with other vaccines. Do not mix it with any other vaccine in the same syringe or vial.
- Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to Human papillomavirus bivalent (Types 16 and 18) vaccine.
- The use of immunoglobulin or blood products should be avoided within 3 months prior to the vaccination of HPV vaccine.
- There has been no clinical evidence available to demonstrate whether the use of hormonal contraceptives will affect the preventive effect of HPV vaccine.
- Like other vaccines, vaccination of HPV vaccine in immunocompromised people may not induce adequate immune response. Concomitant use with immunosuppressive agents may not induce an optimal active immune response.
- At present, there has been no clinical data available to support the interchangeable use among HPV vaccines.
- The injection of HPV vaccine combined with other medicinal products is prohibited.

4.6 Pregnancy and lactation

4.6.1 Pregnancy

At present, there has been no independent study conducted to systematically evaluate the effect on pregnant women. The very limited data from the clinical trial showed that the accidental vaccination during pregnancy does not cause abnormal pregnancy outcomes and neonatal health conditions, and no adverse effects on pregnancy rate, pregnancy outcomes and neonatal health conditions were observed after the vaccination of HPV vaccine. However, the data are not sufficient to determine whether pregnant women are at risk of adverse pregnancy (including spontaneous abortion) after the vaccination. In animal experiments, no direct or indirect adverse effects on reproduction, pregnancy, embryo/fetus development, parturition or postnatal development are observed after the vaccination. Vaccination should be avoided during pregnancy. If a woman is pregnant or preparing for pregnancy, it is recommended to postpone or interrupt the vaccination procedure, and the vaccination can be conducted after the end of pregnancy.

4.6.2 Breast-feeding

There has been no relevant study data to HPV vaccine. As many drugs can be secreted in breast milk, HPV vaccine should be used with caution in lactating women.

4.6.3 Fertility

No fertility data are available

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed. However, some of the effects mentioned under section 4.8 “Undesirable effects” may temporarily affect the ability to drive or use machines

4.8 Undesirable effects

Human papillomavirus bivalent (Types 16 and 18) vaccine is generally well tolerated. The most common local adverse reactions were pain, redness, and swelling at the injection site. The most common general adverse events were fatigue, headache, myalgia, gastrointestinal symptoms, and arthralgia.

4.8.1 Systemic Adverse Reactions

- Very common: Fever (≥37.1 °C)
- Common: Headache, fatigue, cough, muscle pain, nausea, diarrhea, dizziness and vomiting
- Occasional: Hypersensitivity, allergic dermatitis, rash, dizziness and pruritus

4.8.2 Local Adverse Reactions

- Very common: Pain at the injection site
- Common: Pruritus, induration, swelling and erythema at injection site
- Occasional: Rash and discomfort at injection site

Most of the above adverse reactions are mild to moderate.

4.9 Overdose

Not applicable

5. Pharmacological properties

5.1 Pharmacodynamic properties

5.1.1 Pharmacotherapeutic group:

Vaccines, Papillomavirus vaccines

5.1.2 Mechanism of action

Papilovax is an adjuvanted non-infectious recombinant vaccine prepared from the highly purified virus like particles (VLPs) of the major capsid L1 protein of oncogenic HPV types 16 and 18. Since the VLPs contain no viral DNA, they cannot infect cells, reproduce or cause disease. Animal studies have shown that the efficacy of L1 VLP vaccines is largely mediated by the development of a humoral immune response.

5.2 Pharmacokinetic properties2

Not applicable to vaccine products.

6. Pharmaceutical Particulars

6.1 List of excipients

Aluminum Hydroxide, Sodium dihydrogen phosphate, Disodium hydrogen phosphate, Sodium chloride, Polysorbate 80 & Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

- Keep out of the reach and sight of children
- Store and transport at +2 ^{O}C to +8 ^{O}C
- Protect from light

6.5 Nature and contents of container

- Pre-filled syringe 0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (rubber butyl) without needles.

- Pack sizes of 1 pre-filled syringes without needles

6.6 Special precautions for disposal and other handling

A fine white deposit with a clear colorless supernatant may be observed upon storage of the syringe. This does not constitute a sign of deterioration. The content of the 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

7. Marketing authorization holder

Incepta Pharmaceuticals Ltd.

Vaccine Division
Savar, Dhaka
Bangladesh

8. Drug authorization number(s)

Papilovax 0.5 ml PFS- 363- 41-061

9. Date of first authorization /renewal of the authorization

Oct, 2021

10. Date of revision of the text

Oct, 2026