1. NAME OF THE MEDICINAL PRODUCT AND STRENGTH

1.1 Brand Name : HPvax Injection
1.2 Generic Name : Recombinant Human Papillomavirus Vaccine (Types 16, 18) BP.
1.3 Strength : Each 0.5 mL dose contains 40 µg (80 µg/mL) of the recombinant HPV16 protein antigen and 20 µg (40 µg/mL) of the recombinant HPV18 protein antigen.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml contains:

Recombinant Human Papillomavirus Vaccine 16 L1 Protein	:	0.040 mg
Recombinant Human Papillomavirus Vaccine 18 L1 Protein	:	0.020 mg
Aluminum Hydroxide	:	0.600 mg
Sodium Chloride	:	8.800 mg
Polysorbate 80	:	0.050 mg
Sodium Dihydrogen Phosphate Dihydrate	:	0.210 mg
Disodium Hydrogen Phosphate Dihydrate	:	0.120 mg
Water for Injection	:	q.s

3. PHARMACEUTICAL FORM

3.1 The Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine is manufactured by mixing purified HPV16 antigen bulk and purified HPV18 antigen bulk with aluminum adjuvant, to make bivalent antigen adsorbed bulk. The finished drug product is sterile white suspension filled into vials which administrated intramuscularly.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

HPvax is a vaccine indicated for the prevention of the following diseases caused by oncogenic Human Papillomavirus (HPV) types 16 and 18:

- Cervical cancer
- Cervical intraepithelial neoplasia (CIN) Grade 2 or worse and adenocarcinoma.
- Cervical intraepithelial neoplasia (CIN) Grade 1

4.2 Posology and Method of Administration

4.2.1 Dosage

Age at the time of first Injection	Immunization and Schedule
9 to and including 14 years	2 doses 2nd dose 6 month after 1st dose or 3 doses at 0,1 and 6 months
From 15 years and above	3 doses at 0,1 and 6 months

The need for a booster dose has not been established. If flexibility in the vaccination schedule is necessary, the second dose can be injected within 1-2 month after the first dose, 3rd dose can be injected within 5-8 months after the first dose.

4.2.2 **Method of Administration**

HPvax should be given intramuscularly in the deltoid region of arm in female aged from 9 years. The vaccine should be well shaken before use. The suspension should be used as supplied, no dilution or reconstitution process is needed. Once the vial is opened, the preparation must be used immediately.

4.3 Contraindications

The vaccine should not be given to person who is hypertensive to any of the substances mentioned in composition. Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to HPvax.

4.4 Special warnings and precaution for use

4.4.1 Because vaccines may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure like activity.

4.4.2 HPvax will only protect against disease that are caused by HPV type 16, 18 and to some extent against diseases caused by certain other oncogenic related HPV types. Therefore, appropriate precautions against sexually transmitted diseases should continue to be used.

4.4.3 HPvax is for prophylactic use only and has no effect on active HPV injections. Therefore, the vaccine is not indicated for treatment of cervical cancer or cervical neoplasia (CIN).It is also not intended to prevent progression of other established HPV related lesions or existing injections with vaccine and non-vaccines types.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

4.5.1 Immunosuppressive therapies may reduce the immune response to vaccines.

4.5.2 Do not mix HPvax Injection with any other vaccine in the same syringe or vial.

4.6 Fertility,Pregnancy and Lactation

4.6.1 **Pregnancy:** Pregnancy category B, reproduction studies have been performed in rats at a dose approximately 47 times the human dose (on mg/kg basis) and revealed no evidence of impaired fertility or harm to the fetus due HPV vaccine. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this vaccine should be used during pregnancy only if clearly needed.

4.6.2 **Lactation:** The effect on breast-fed infants of the administration of HPV vaccine to their mothers has not been evaluated in clinical studies. HPV vaccine should only be used during breast – feeding when the possible advantages outweigh the possible risks.

4.7 Effects on Ability to Drive and Use Machines

4.7.1 No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

4.8.1 Most common local adverse reactions in ≥20% of subjects were pain, redness and swelling at the injection site.

4.8.2 Most common general adverse events in ≥20% of subjects were fatigue, headache, myalgia, gastrointestinal symptoms and arthralgia.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

This section is not applicable for this product

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccine.

5.3 Preclinical safety Data

During observation period of Acute Toxicity Study of Intramuscular Injection of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine in Rats, no animals in 0 mg/kg or 1.2 mg/kg dose group showed obvious symptoms of toxicity or death, and weight gain of the animals was not inhibited. At the end of observation, gross anatomy was performed for all the test animals. There was no abnormality in major tissue, organs, skin or muscle of injection site.

Immunotoxicity study of repeated intramuscular injection of HPvax Injection induced no toxic pathological change in heart, liver, spleen, lung, kidney, brain, reproductive system, intramuscular injection site, lymph nodes or other organs or tissue of SD rats under the conditions of this study.

Under the conditions of the study, intramuscular injection of HPvax Injection to rats induced no significant adverse reactions in pregnant Wistar rats, showed no significant impact on body weight or food intake of pregnant rats, and showed no maternal toxicity, fetal toxicity or teratogenic effects on appearance, viscera or bones of fetal rats.

Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (*Escherichia. coli*) was negative in systemic allergy study in guinea pigs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminum Hydroxide
Sodium Chloride
Polysorbate 80
Sodium Dihydrogen Phosphate Dihydrate
Disodium Hydrogen Phosphate Dihydrate

6.2 Incompatibilities

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

6.3 Shelf Life

3 years

6.4 Special precautions for storage

6.4.1 Keep out of the reach and sight of children.
6.4.2 Store and transport at 2 ºC to 8 ºC.
6.4.3 Do not freeze. Discard vaccine if frozen.
6.4.4 Protect from light

6.5 Nature and contents of container and special equipment for use ,administration or implantation

HPvax lyophilized Injection is filled in USP Type I glass vials closed bromobutyl rubber stoppers and sealed with aluminium flip-off seals. The liquid vial (single dose) is presented in a plastic tray along with 2 ml sterile disposable syringe.

6.6 **Special precautions for disposal and other handling**

6.6.1 Discard if the vaccine has been frozen.

6.6.2 The vaccine should be inspected visually in order to detect any appearance of precipitate or discoloring of the content prior to administration. If these conditions exist, the product should not be administered.

6.6.3 Once the vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.

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

7. MARKETING AUTHORIZATION HOLDER NAME AND ADDRESS

Head Office Address:

Popular Pharmaceuticals Ltd.
Sheltech Panthokunjo, 17 Shukrabad, West Panthopath, Dhaka - 1207, Bangladesh
Email: info@popularbd.com
Phone: +880-2-9101730-2, +880-2-9102850-3
Fax: +880-2-9134054, +880-2-9134096
Mobile: +880-1833332352-55

Factory Address:

Popular Pharmaceuticals Ltd.
164, Tongi Industrial Area, Monnunagar,
Gazipur – 1710, Bangladesh
Email: info@popularbd.com
Phone: +880-2-9812971-5
Fax: +880-2-9812976

8. DRUG AUTHORIZATION NUMBER

MA No.: 336 – 781– 069

9. DATE OF FIRST AUTHORIZATION /RENEWEL OF AUTHIRIZATION

Date of First Authorization : 08.02.2022
Date of Latest Renewal : NA

10. DATE OF REVISION OF THE TEXT

08.08.2023