HUMAN PAPILLOMAVIRUS (HPV)

BIOSUN PHARMED VACCINE (GARDISUN™)

Based on WHO Guidelines, Gardisun™ considered a very similar vaccine to Gardasil®.

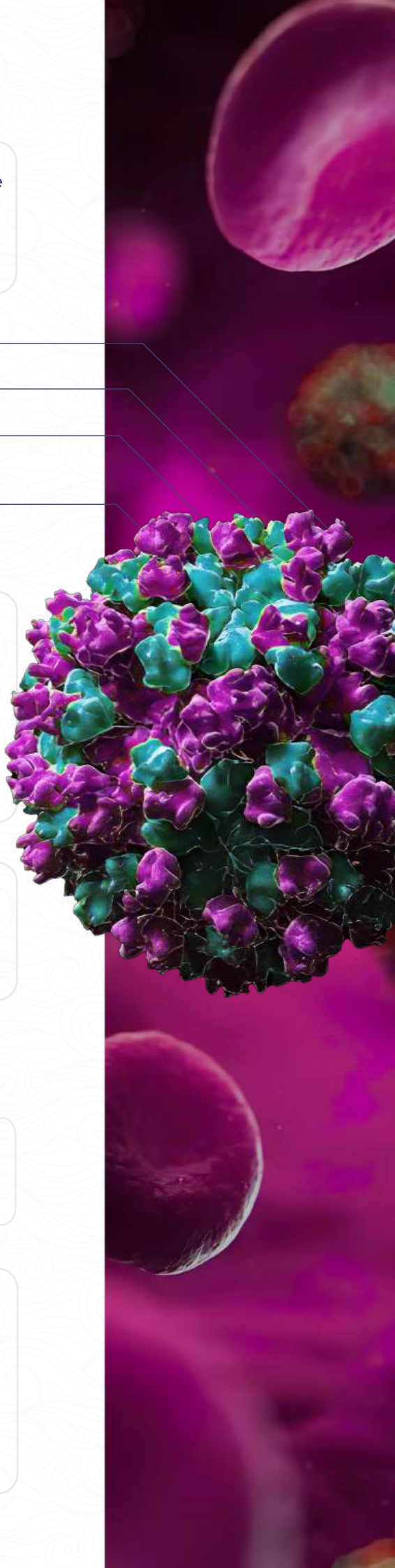
- Recombinant, Adsorbed & Quadrivalent HPV vaccine [serotypes 6 ,11 ,16 ,18 L1 protein]

The highly purified virus-like particles (VLPs)

Engineered H. polymorpha serves as a host cell

Adsorbed on AAHS adjuvant

The sequence of Purified Protein L1 is very similar to L1 sequences published on National Center for Biotechnology Information (NCBI)



PRECLINICAL STUDIES

Gardisun™ vs. Gardasil®

- *Cellular immunity*
- *Humoral immunity*
- *Single-Dose & Repeat-Dose Toxicity*
- *Reproductive & Developmental Toxicity*
- *Local Tolerance in Rat*

Gardisun™ and Gardasil® both behave similarly in all studies.

VACCINE DOSAGE FORM

Gardisun™ is a single dose pre-filled syringe of 0.5 mL sterile liquid suspension. Each dose contains 20 µg of HPV 6 L1 protein, 40 µg of HPV 11 L1 protein, 40 µg of HPV 16 L1 protein, 20 µg of HPV 18 L1 protein.

CLINICAL TRIAL SUMMARY

Gardisun™ vs. Gardasil® Phase III clinical trial

The Phase III, randomized, double-blinded, active-controlled non-inferiority trial to evaluate the immunogenicity and safety of papillomavirus vaccine (6 ,11 ,16 ,18)

All aspects of this study adhere to the principles of the World Health Organization (WHO) Technical Report Series No.999, annex 4, and ICH GCP

- *Healthy volunteers aged 15-35 years*
- *450 male & female participants*
- *Baseline seronegative for antibody titers against HPV*
- *7 months follow-up duration*
- *3 dose vaccines (according to 0, 2, 6 schedule)*
- *Antibody titration by USA-Alpha diagnostic ELISA kit*

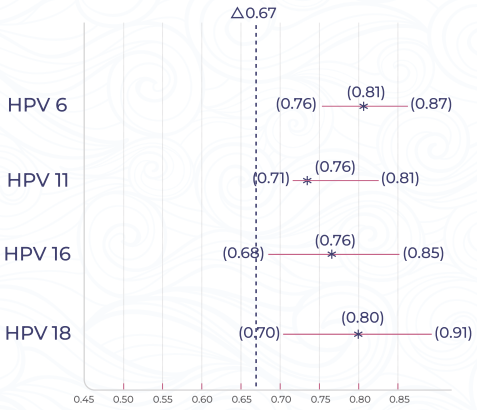
World Health Organization

Main Outcomes

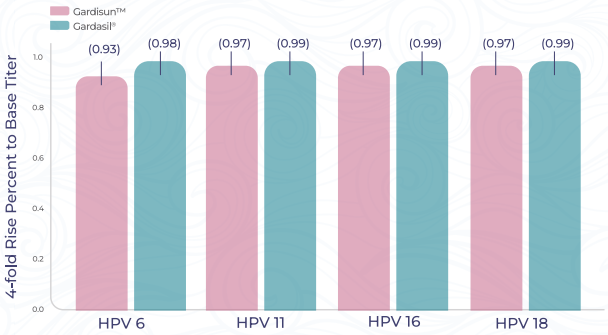
- The antibody levels against HPV types 6 ,11 ,16, and 18 were measured using geometric mean titers (GMT)
- Immune responses to the vaccine were evaluated focusing on seroconversion rates.
- Local, systemic acute, and allergic adverse events (Solicited and Unsolicited) were assessed.

According to the WHO guideline, the non-inferiority of Gardisun™ to Gardasil® has been confirmed in terms of immunogenicity based on the GMT ratio. Seroconversion rate in both groups has been assessed by 4-fold rise of antibody titer compared to baseline. Additionally, the safety profile of Gardisun™ was comparable to that of Gardasil®.

Symptom (>%10)	Gardisun™	Gardasil®
Injection Site Pain	41.2	32.1
Rhinitis	19.5	21.9
Headache	20.8	17.4
Pharyngitis	17.3	17.4
Myalgia	14.2	14.7
Pyrexia	15.9	10.7
Coughing	11.5	10.3
Asthenia	11.1	10.3



Geometric Mean Titer Ratio
(IQR method, CI 95%)



Seroconversion Rate
(CI 95%)

PHARMACOVIGILANCE

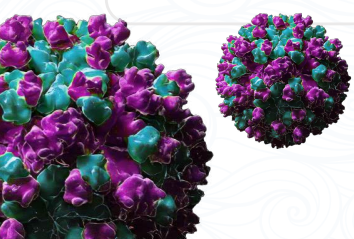
Detection, assessment, and prevention of ADRs which is possible only through the pharmacovigilance system is of great importance. Also, training programs are part of Gardisun™ pharmacovigilance process which results in the rational and more effective use of the vaccine, and better adherence within the target population.

60 guidelines including GVP, ICH, CIOMS (WHO) guidelines and internal standard procedures were reviewed for Gardisun™ vaccine pharmacovigilance system establishment.

Healthcare professionals (HCPs), IFDA and consumers are involved partners in Gardisun™ vaccine pharmacovigilance system.

Constant surveillance through pharmacovigilance system results in

- *Detection and prevention of ADRs, Interactions and medication errors*
- *Tracking counterfeit medicines*
- *Fast and efficient decision-making in risk situations*



GARDISUN
[serotypes 6, 11, 16, 18 L1 protein]
(Recombinant, Adsorbed)

BIOSUN PHARMED
بیوسان فارمد