



# Pharmacy Bulletin



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## UPDATES ON HPV-9 VACCINES

The Human Papilloma Virus (HPV) is a group of more than 130 subtypes of HPV, and about 70 subtypes infect human. Out of these, about 40 different genotypes of HPV can infect the ano-genital area in men and women which can lead to cervical, vaginal and vulvar cancers in women and penile cancers in men. HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide. Based on molecular biological and epidemiological studies, the genital HPV types are classified as follows:





<b>High Risk</b>	HPV types <b>16, 18, 31, 33</b> , 35, 39, <b>45</b> , 51, <b>52</b> , 56, <b>58</b> , 59
<b>Probable High</b>	HPV types 26, 53, 66, 68, 73, 82
<b>Low Risk</b>	HPV types <b>6, 11</b> , 40, 42, 43, 44, 54, 61, 70, 72, 81, CP6108

Pap smear remains the main screening form for this cancer, however it is not cost effective to screen for HPV in women younger than 30 years old. Hence, vaccination is the best alternative to prevent the disease from occurring. (HPV) vaccine first arrived at the Malaysian shore in 2006 under the brand Gardasil, marketed by Merck, Sharp & Dohme (MSD). The quadrivalent vaccine covers for subtype 6, 11, 16 and 18. Subsequently, Glaxo Smith & Kline (GSK) launched their **bivalent** HPV vaccine the following year, marketed as Cervarix that contains subtype 16 and 18. Starting 2010, the government has implemented the **National HPV Immunisation Programme (NIP)** that gives free supply of HPV vaccine to 13 year olds female.

According to a published data by ICO Information Centre on HPV and Cancer 2017, Malaysia has a population of 12 millions women ages 15 years and older who are at risk of developing cervical cancer. It is estimated that 2,145 women are diagnosed with cervical cancer every year and 621 die from the disease. Cervical cancer ranks as the second leading cause of female cancer deaths in Malaysia and is the second leading cause of cancer deaths in women aged 15 to 44 years in Malaysia. About 1% of women in the general population are estimated to harbour cervical HPV-16/18 infection at a given time, and 88.7% of invasive cervical cancers are attributed to HPVs 16 or 18. Below are the key statistics of HPV in Malaysia <sup>1</sup>:

<b>Population</b>		
Women at risk for cervical cancer (Female population aged >=15 years)		12.0 million
<b>Burden of cervical cancer and other HPV-related cancers</b>		
Annual number of cervical cancer cases		2,145
Annual number of cervical cancer deaths		621
Crude incidence rates per 100,000 and year:	<b>Male</b>	<b>Female</b>
Cervical cancer	-	14.8
Anal cancer ‡	0.0-0.3	0.2-0.3
Vulvar cancer ‡	-	0.2-0.7
Vaginal cancer ‡	-	0.2-0.7
Penile cancer ‡	0.1-0.7	-
Pharynx cancer (excluding nasopharynx)	1.4	0.6
<b>Burden of cervical HPV infection</b>		
Prevalence (%) of HPV 16 and/or HPV 18 among women with:	<b>Normal cytology</b>	1.0
	<b>Low-grade cervical lesions (LSIL/CIN-1)</b>	30.4
	<b>High-grade cervical lesions (HSIL/CIN-2/CIN-3/CIS)</b>	49.3
	<b>Cervical cancer</b>	88.7
<b>Other factors contributing to cervical cancer</b>		
Smoking prevalence (%), women		1.5 [1.0-2.2]
Total fertility rate (live births per women)		2.1
Oral contraceptive use (%) among women		13.2
HIV prevalence (%), adults (15-49 years)		0.4 [0.3 - 0.5]
<b>Sexual behaviour</b>		
Percentage of 15-year-old who have had sexual intercourse (men/women)		- / -
Range of median age at first sexual intercourse (men/women)		- / -
<b>Cervical screening practices and recommendations</b>		
Cervical cancer screening coverage, % (age and screening interval, reference)	22.2% (All women aged 20-65 screened every 1y, Annual Report 2012 Malaysia)	
Screening ages (years)		20-65
Screening interval (years) or frequency of screens		3 years

An 'upgraded' version of Gardasil called Gardasil 9 is currently available in Malaysia after its recent launch in 2017. Gardasil 9 consists 9 types of HPV (7 from the high risk subtype ie 16,18,31,33,45,52 and 58) and another 2 from the low risk subtype (ie 6 and 11). The differences among the 3 HPV vaccines available in Malaysia are as follow :

	Bi-valent (2VHPV)	Quad-rivalent (4VHPV)	Nona--valent (9VHPV)											
<b>Brand</b>	<b>Cervarix</b> 	<b>Gardasil</b> 	<b>Gardasil 9</b> 											
<b>Manufacturer</b>	Glaxo Smith Kline (GSK)	Merck, Sharp & Dohme (MSD)												
<b>HPV types included</b>	16, 18 (high risk)	16, 18 (high risk) 6, 11 (low risk) - genital warts	16,18,31,33,45,52 and 58 (high risk) 6, 11 (low risk) - genital warts											
<b>Gender &amp; Age for vaccination</b>	Females 9-26 yo	Females & males 9-26 yo	Females 9-26 yo , Males 9-15 yo											
<b>Dosing schedule</b>	3 doses over 6 months (0, <b>1</b> , 6 months)	3 doses over 6 months (0, <b>2</b> , 6 months)	<table border="1"> <thead> <tr> <th>Age (yo)</th> <th>Regimen</th> <th>Schedule</th> </tr> </thead> <tbody> <tr> <td rowspan="2"><b>9-14</b></td> <td>2-dose</td> <td>0, 6-12 mo</td> </tr> <tr> <td>3-dose</td> <td>0, 2, 6 mo</td> </tr> <tr> <td><b>15-26</b></td> <td>3-dose</td> <td>0, 2, 6 mo</td> </tr> </tbody> </table> <p>If the second dose is administered earlier than 5 months after the 1st dose, administer a 3rd dose at least 4 months after the second dose.</p>	Age (yo)	Regimen	Schedule	<b>9-14</b>	2-dose	0, 6-12 mo	3-dose	0, 2, 6 mo	<b>15-26</b>	3-dose	0, 2, 6 mo
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<b>Administration</b>	0.5 mL as Intramuscular injection (IM) only at the deltoid region of the upper arm or in the higher anterolateral area of the thigh													
<b>Protection against</b>	Cervical cancer	<b>Cervical cancer</b> : (HPV 16– and 18– related *CIN 2/3 or AIS) : <b>98%</b> efficacy <b>Vulvar &amp; vaginal cancer</b> : ( HPV 16– and 18– related VIN 2/3 and VaIN 2/3): <b>100 %</b> efficacy <b>Anal cancer</b> : (HPV 6-, 11-, 16– , 18– and related AIN 2/3) : <b>75%</b> Efficacy <b>Genital warts</b> : HPV 6– and 11– related : <b>89%</b> in ♂ , <b>99%</b> in ♀												
<b>Production of VLPs</b>	Insect cells infected with recombinant <b>baculovirus</b>	Yeast cells ( <i>Saacharomyces cerevisiae</i> ) with recombinant <b>plasmid</b>												
<b>Adjuvant</b>	<b>ASO4</b> [500 mcg of Aluminum hydroxide plus 50 mcg of Monophosphoryl Lipid A]	<b>AAHS</b> 225mcg of Amorphous Aluminum Hydroxyphosphate Sulfate, 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate,												
<b>Contra-indications</b>	Hypersensitivity to <b>latex</b>	Hypersensitivity to <b>yeast</b>												
<b>Precautions</b>	Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following HPV vaccination. Observation for 15 minutes after administration is recommended. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position.													

**Note :**

\*\* AIS : Anal Intraepithelial Neoplasia

\*CIN : Cervical Intraepithelial Neoplasia

**References:**

1) ICO/IARC Information Centre on HPV and Cancer

3) <http://www.e-mjm.org/2014/supplement-A/cervical-cancer-research.pdf>

2) <https://www.merckvaccines.com/Products/Gardasil9>

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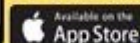
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