Gardasil 9 – A Broader HPV Vaccine

The FDA has now approved a recombinant, 9-valent, human papillomavirus (HPV) vaccine (Gardasil 9 – Merck) for use in girls and women 9-26 years old and boys 9-15 years old. The new vaccine is indicated to prevent diseases associated with infection with HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, which include genital warts and cervical, vulvar, vaginal, and anal precancerous lesions and cancer. Two recombinant HPV vaccines are already available in the US: Gardasil prevents disease associated with HPV types 6, 11, 16, and 18,1 and Cervarix prevents disease associated with HPV types 16 and 18.2

HPV INFECTION — HPV is commonly acquired by young women soon after initiation of sexual activity, with a cumulative incidence of 40% within 16 months. Although most HPV infections clear spontaneously without clinical sequelae, persistent infection can cause abnormalities in the cervical epithelium that may progress to cancer. HPV types 16 and 18 are responsible for approximately 70% of cervical cancers. The five HPV types added to the 9-valent vaccine – 31, 33, 45, 52, and 58 – are responsible for an additional 15-20% of cervical cancers.3 Types 6 and 11 cause more than 90% of genital warts.4

CLINICAL STUDIES — The efficacy and immunogenicity of Gardasil 9 were evaluated in a randomized, double-blind trial in 14,215 previously unvaccinated females 16-26 years old who were given a dose of either the 9-valent or the quadrivalent HPV vaccine (Gardasil) on day 1 and again at months 2 and 6. Compared to the quadrivalent vaccine, Gardasil 9 reduced the risk of high-grade cervical, vulvar, or vaginal disease related to HPV types 31, 33, 45, 52, or 58 by 97% (0.1 vs. 1.6 cases/1000 person-years) after a median of 40 months following the last vaccination. Antibody responses to the 4 HPV types found in both vaccines (HPV types 6, 11, 16, and 18) were similar with Gardasil and Gardasil 9, as was the incidence of disease or persistent infection related to those HPV types.5

The effectiveness of Gardasil 9 for children 9-15 years old was inferred from an unpublished immunogenicity study (summarized in the package insert) that found antibody responses in girls and boys 9-15 years old to be noninferior to those in girls and women 16-26 years old.

An unpublished study in females 12-26 years old who were previously vaccinated with the quadrivalent vaccine found that administration of 3 doses of Gardasil 9 resulted in seropositivity to the five additional HPV types in more than 98% of the subjects, but anti-HPV titers for those types were 25-63% of those reported in previously unvaccinated subjects given the new vaccine; the clinical significance of these differences is unknown.

Table 1. HPV Vaccines

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>HPV Types</th>
<th>Formulations</th>
<th>Dose/Schedule</th>
<th>Cost1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervarix (GSK)</td>
<td>16 and 18</td>
<td>0.5 mL single dose syringes2</td>
<td>0.5 mL IM/3 doses (0, 1, and 6 months)</td>
<td>$384.00</td>
</tr>
<tr>
<td>Gardasil (Merck)</td>
<td>6, 11, 16, and 18</td>
<td>0.5 mL single dose vials2</td>
<td>0.5 mL IM/3 doses (0, 2, and 6 months)</td>
<td>443.30</td>
</tr>
<tr>
<td>Gardasil 9 (Merck)</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, and 58</td>
<td>0.5 mL single dose vials2</td>
<td>0.5 mL IM/3 doses (0, 2, and 6 months)</td>
<td>491.60</td>
</tr>
</tbody>
</table>

1. Approximate WAC for 1 series (3 doses). WAC = wholesaler acquisition cost or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. March 5, 2015. Reprinted with permission by First Databank, Inc. All rights reserved. ©2015. www.fdbhealth.com/policies/drug-pricing-policy.
2. Sold in packages of 10 single-dose prefilled syringes.
3. Sold in cartons of 1 or 10 single-dose vials or 6 or 10 single-dose prefilled syringes.
4. Sold in cartons of 1 or 10 single-dose vials or 10 single-dose prefilled syringes.

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ADVERSE EFFECTS — Injection-site reactions are common, slightly more so with Gardasil 9 than with the quadrivalent vaccine (91% vs. 85%). Syncope has occurred after administration of HPV vaccines; patients should be seated and observed for 15 minutes after the injection.

RECOMMENDATIONS — The US Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination with the bivalent or quadrivalent vaccine for girls 11-12 years old and with the quadrivalent vaccine for boys 11-12 years old. Vaccination is also recommended for females 13-26 years old and males 13-21 years old who have not been vaccinated previously (immunocompromised men and men who have sex with men should be vaccinated through age 26).

Specific recommendations regarding use of the 9-valent HPV vaccine have not been published yet, but the ACIP voted at a recent meeting to add Gardasil 9 to its recommendations for HPV vaccination, which will probably include the possibility of using it to complete a vaccine series started with another HPV vaccine.

CONCLUSION — The new HPV vaccine, Gardasil 9, should be more effective than Gardasil or Cervarix in preventing cervical and other genital cancers. It will probably replace the currently marketed quadrivalent vaccine.