

# Bivalent HPV Recombinant Vaccine (Cervarix) for the Prevention of Cervical Cancer

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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The bivalent human papillomavirus (HPV) recombinant vaccine (Cervarix) is the second vaccine to be approved in the United States for the prevention of cervical cancer, cervical adenocarcinoma in situ, and cervical intraepithelial neoplasia (CIN) caused by HPV types 16 and 18.<sup>1</sup> These HPV types currently cause 70 percent of all cervical cancers.<sup>2</sup> Unlike the quadrivalent HPV vaccine (Gardasil), Cervarix does not provide protection against HPV types 6 and 11, which are responsible for 90 percent of genital warts in males and females.<sup>2</sup> The Advisory Committee on Immunization Practices recommends HPV vaccination for females nine to 26 years of age.<sup>2</sup>

<i>Drug</i>	<i>Starting dosage</i>	<i>Dose form</i>	<i>Approximate monthly cost*</i>
Bivalent human papillomavirus recombinant vaccine (Cervarix)	A series of three intramuscular 0.5-mL doses, with the second dose given at least one month after the initial dose and the third dose given at least six months after the initial dose	0.5-mL single-dose vial or 0.5-mL single-dose prefilled syringe	\$154 per dose \$462 for the three-dose series

\*—Average wholesale cost based on Red Book. Montvale, N.J.: Medical Economics Data; 2010.

## SAFETY

Safety concerns include minor injection site reactions and general adverse effects similar to those of other vaccines. The tip cap and rubber plunger of the needleless prefilled syringes contain dry natural latex rubber that may cause an allergic reaction in latex-sensitive persons.<sup>1</sup> Cervarix is not a live vaccine; therefore, it can be administered with or at any time before or after other inactivated or live vaccines.<sup>2</sup> It is U.S. Food and Drug Administration pregnancy category B; however, the manufacturer does not recommend its use in pregnant women.

## TOLERABILITY

Cervarix was well tolerated in clinical trials of more than 16,000 females. Minor injection site reactions were common and included

pain (91.8 percent), redness (48 percent), and swelling (44.1 percent). Reports of fatigue (55 percent), myalgia (49 percent), arthralgia (21 percent), and urticaria (7 percent) were also common, although these effects did not increase in frequency with successive doses.<sup>1</sup> In approximately 6,400 patients receiving the vaccine, 28 percent reported gastrointestinal symptoms of nausea, vomiting, diarrhea, and abdominal pain, and 13 percent developed a fever within seven days of vaccination.<sup>1</sup> These rates of adverse effects are similar to those reported by patients receiving a control vaccine (hepatitis A).<sup>1</sup>

## EFFECTIVENESS

In patients without HPV infection, Cervarix will prevent CIN grades 1 and 2 caused by HPV types 16 and 18, and in patients who ►

have lesions independent of HPV DNA, it will decrease the likelihood of developing CIN grade 2 or higher by 71 percent (effectiveness: 71 percent; 95% confidence interval, 20.6 to 91.9).<sup>3</sup> As with Gardasil, Cervarix has not been shown to prevent cervical cancer.

Whether patients had previous or ongoing HPV infection, Cervarix was 93 percent effective (95% confidence interval, 87 to 96) in preventing cytologic and histologic cervical lesions (CIN grades 1 to 3), or adenocarcinoma in situ in a follow-up of 14 to 44 months.<sup>4</sup> One additional patient is prevented from developing CIN grade 2 or 3 lesions for every 411 patients who receive the vaccine.

In the single head-to-head comparison of Cervarix and Gardasil, anti-HPV 16 and 18 neutralizing antibody titers were several-fold higher with Cervarix at one month after completion of the series. Whether this increased response results in improved prevention of cervical dysplasia or cancer is not known.<sup>5</sup>

#### PRICE

The cost of Cervarix is \$154 per dose and \$462 for a three-dose series. The cost of Gardasil is \$145 per dose and \$436 for a three-dose series.<sup>6</sup>

#### SIMPLICITY

The recommended dosing schedule for Cervarix is a series of three doses, with the second dose given at least one month after the initial dose and the third dose given at least six months after the initial dose. This differs slightly from the schedule of Gardasil, which is given at zero, two, and six months. If the Cervarix schedule is interrupted, the series does not need to be restarted.<sup>2</sup> Cervarix is recommended for girls 11 to 13 years of age, although it can be administered to those as young as nine years.<sup>2</sup> It is available in a single-dose 0.5-mL vial or 0.5-mL single-dose prefilled syringe and should be administered intramuscularly into the deltoid region of the upper arm. The vaccine should be

refrigerated and the suspension should be shaken before administration.<sup>1</sup>

#### Bottom Line

Cervarix is effective in preventing known cytologic and histologic precursors of cervical cancer, although, as with Gardasil, it has not been shown to decrease rates of cervical cancer. This protection has been shown to last for six years, but it is unclear if a booster dose is needed. Cervarix does not protect against the two strains of HPV responsible for genital warts and is of no value in males. Vaccination with either HPV vaccine does not remove the need, at this time, for continued regular cervical cancer screening.

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