Easy Choice Health Plan, Inc.
Exactus Pharmacy Solutions, Inc.
Harmony Health Plan of Illinois, Inc.
Missouri Care, Incorporated
WellCare Health Insurance of Arizona, Inc., operating in Hawai‘i as ‘Ohana Health Plan, Inc.
WellCare of Kentucky, Inc.
WellCare Health Plans of Kentucky, Inc.
WellCare Health Plans of New Jersey, Inc.
WellCare of Connecticut, Inc.
WellCare of Florida, Inc., operating in Florida as Staywell
WellCare of Georgia, Inc.
WellCare of Louisiana, Inc.
WellCare of New York, Inc.
WellCare of South Carolina, Inc.
WellCare of Texas, Inc.
WellCare Prescription Insurance, Inc.
Windsor Health Plan, Inc.

**HPV Vaccine for Males**

**Policy Number:** HS-198

**Original Effective Date:** 1/5/2012

**Revised Date(s):** 12/6/2012; 1/9/2014; 1/8/2015; 1/7/2016

**APPLICATION STATEMENT**

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

Clinical Coverage Guideline

Original Effective Date: 1/5/2012  Revised: 12/6/2012, 1/9/2014, 1/8/2015, 1/7/2016
DISCLAIMER
The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member’s Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. Note: Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com – select the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND
Genital human papillomavirus (HPV) is the most common sexually transmitted virus in the US. More than 50% of sexually active men and women are infected with HPV at some time in their lives. There are about 40 different types of HPV that can cause infection. Some types can cause serious health problems such as cervical cancer in women, other cancers in the genital area in women and men, and genital warts in women and men. HPV vaccine can prevent most genital warts and most cases of cervical cancer. (American Academy of Pediatrics, 2011a). According to the Centers for Disease Control and Prevention (2011b), approximately 20 million Americans are currently infected with HPV. Annually, 18,000 HPV associated cancers affect women in the U.S. (cervical is the most common type). Among U.S. men, 7,000 are diagnosed with an HPV associated cancer; cancers of the head and neck most common. HPV can cause genital warts in men and women; about 1 in 100 sexually active adults in the U.S. has genital warts at any one time. Men who have sex with men and people who are infected with HIV are at the highest risk for HPV–related disease.

In October 2011, the CDC Advisory Committee on Immunization Practices (ACIP) recommended routine use of quadrivalent human papillomavirus (HPV) vaccine (HPV4; Gardasil, Merck & Co., Inc.) in males aged 11 and 12 years. The vaccine should be given in a 3-dose series which can begin at age 9. ACIP also recommended vaccination with HPV4 for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated. (Hayes, 2011; CDC, 2011a). HPV4 is not a live vaccine and can be administered to persons who are immunocompromised as a result of infection (including HIV), disease, or medications. The immune response and vaccine efficacy might be less than that in immunocompetent persons. For immunocompromised males, ACIP recommends routine vaccination with HPV4 as for all males, and vaccination through age 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated. (Hayes, 2011; CDC, 2011a). HPV4 is not a live vaccine and can be administered to persons who are immunocompromised as a result of infection (including HIV), disease, or medications. The immune response and vaccine efficacy might be less than that in immunocompetent persons. For immunocompromised males, ACIP recommends routine vaccination with HPV4 as for all males, and vaccination through age 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated. (Hayes, 2011; CDC, 2011a).

Safety. Clinical trial data in approximately 5,300 males found that the most common adverse events were mild or moderate, and were most commonly injection-site reactions (FDA, 2011). Headache and fever were the most commonly reported systemic adverse events in vaccine recipients and controls (FDA, 2011). ACIP recommends that vaccination providers should consider observing patients for 15 minutes after all vaccinations, including HPV.

Special Populations. MSM are at higher risk for conditions associated with HPV types 6, 11, 16, and 18 than are heterosexual men; diseases and cancers that have a higher incidence among MSM include AIN, anal cancers, and genital warts (Chin-Hong, 2002; Jin, et al., 2007). HPV4 clinical trial data demonstrated high efficacy for prevention of genital warts, AIN1/2/3, and AIN2/3 (FDA, 2011). HPV4 is not licensed for males aged >26 years, and no information is available on the efficacy for prevention of outcomes in MSM aged >26 years.

Rationale. Although the largest number of HPV-associated cancers occur in women (approximately 15,000 HPV 16- and 18-associated cancers each year), an estimated 7,000 HPV 16- and 18-associated cancers occur each year in men in the United States. These include anal, oropharyngeal, and penile cancers. HPV4 has high efficacy for prevention of genital warts, AIN1/2/3, and AIN2/3 in males. HPV4 also has high efficacy for prevention of genital warts, CIN1/2/3 or AIS, CIN2/3, VIN2/3, and VaIN2/3 in females. Although data show HPV4 prevents various outcomes, no data are available on the efficacy for prevention of oropharyngeal or penile cancers. Vaccination of males would provide direct benefits and likely would reduce HPV 6, 11, 16, and 18 transmission, and resulting infection, disease, and cancers in females (through herd immunity). However, no clinical efficacy data
demonstrating that HPV4 prevents HPV transmission are available. (CDC, 2011a).

Because HPV4 is prophylactic, it would be most effective when given before exposure to HPV through sexual contact. The recommendation for vaccination at ages 11 or 12 years is supported by data from the efficacy trial, demonstrating highest efficacy in males who had no evidence of previous or current HPV vaccine type infection, data on sexual behavior in the United States, and immunogenicity studies showing higher antibody titers after vaccination of males at ages 9 through 15 years compared with those aged 16 through 26 years. Other vaccines are recommended at age 11 or 12 years, including HPV vaccine for females. The population level benefits decrease with increasing age at vaccination, especially after age 21 years.

**POSITION STATEMENT**

**Applicable To:**
- Medicaid – All Markets

Administration of the HPV vaccine for males is considered medically necessary and a covered benefit.

**CLINICAL EVIDENCE**

In a phase III efficacy trial, HPV4 had high efficacy for prevention of genital warts among 4,055 males aged 16 through 26 years. (Exclusion criteria included history of genital warts, history of genital lesions possibly HPV-related, and less than one or more than five lifetime sex partners). Among those who received all 3 vaccine doses and were seronegative at day 1 and DNA-negative day 1 through month 7 to the respective HPV type (per protocol population), efficacy for prevention of HPV 6-, 11-, 16-, and 18-related genital warts was 89.3% (95% confidence interval [CI] = 65.3%–97.9%); efficacy for HPV 6- and 11-related genital warts was similar. Efficacy for prevention of HPV 6-, 11-, 16- and 18-related genital warts among males who received at least 1 vaccine dose, regardless of baseline infection or serology (intent to treat population), was 68.1% (CI = 48.8%–80.7%) (4). No efficacy was observed among males who were infected with the respective HPV type at baseline. Although grade 1, 2, and 3 penile/perineal/perianal intraepithelial neoplasias were evaluated, too few were observed, and efficacy was not demonstrated (FDA, 2011).

A substudy of the phase III efficacy trial included 598 MSM, aged 16 through 26 years; outcomes were genital warts; AIN grades 1, 2, or 3 (AIN1/2/3); and AIN2/3. Per protocol efficacy for prevention of HPV 6-, 11-, 16-, and 18-related genital warts was 88.1% (CI = 13.9%–99.7%) (CDC, 2011). Per protocol efficacy for prevention of HPV 6-, 11-, 16-, and 18-related genital warts among males who received at least 1 vaccine dose, regardless of baseline infection or serology (intent to treat population), was 77.5% (CI = 39.6%–93.3%), and against AIN2/3 was 74.9% (CI = 8.8%–95.4%) (Table) (FDA, 2011). In the intent to treat population, efficacy for prevention of HPV 6-, 11-, 16-, and 18-related AIN1/2/3 was 50.3% (CI = 25.7%–67.2%), and prevention of HPV 6-, 11-, 16-, and 18-related AIN2/3 was 54.2% (CI = 18.0%–75.3%) (FDA, 2011). In the intent to treat population, efficacy for prevention of any HPV type-related AIN2/3 was 24.3% (CI = 13.8%–35.0%) (FDA, 2011). No studies have evaluated the efficacy of HPV4 for prevention of recurrent respiratory papillomatosis or oropharyngeal cancer.

**CODING**

**Covered CPT® Codes**
- 90649 Human Papilloma Virus (HPV) vaccine types 6, 11, 18, (quadrivalent), 3 dose schedule, for IM use
- 90651 HPV vaccine, types 6, 11, 16, 18, 31, 33, 42, 52, 58, nonavalent (9vHPV), 3 doses scheduled for IM use

**ICD-9-CM Procedure Code** – No applicable codes.

**HCPCS Level II® Codes** – No applicable codes.

**Covered ICD-9-CM Diagnosis Codes**
- V04.89 Prophylactic vaccination and inoculation against other viral disease, i.e., HPV

**Covered ICD-10-CM Diagnosis Codes**
- Z23 Encounter for immunization

REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<tr>
<td>1/7/2016</td>
<td>Approved by MPC. No changes.</td>
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<tr>
<td>1/8/2015</td>
<td>Approved by MPC. Coding update.</td>
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<tr>
<td>1/9/2014, 12/6/2012</td>
<td>Approved by MPC. No changes.</td>
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<tr>
<td>1/5/2012</td>
<td>New guideline. Approved by MPC.</td>
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