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FDA adds prevention of oropharyngeal cancer to HPV vaccine's indication

by from the Food and Drug Administration's Office of Pediatric Therapeutics and Center for Drug Evaluation and Research, Division of Pediatric and Maternal Health and Center for Biologics and Research

The human papillomavirus (HPV) recombinant 9-valent vaccine (Gardasil 9) received Food and Drug Administration (FDA) approval for an expanded indication to include the prevention of oropharyngeal and other head and neck cancers caused by HPV types 16, 18, 31, 33, 45, 52 and 58.

Gardasil 9 was licensed in 2014 for prevention of HPV-related cervical, vaginal and vulvar cancers in females and HPV-related anogenital lesions and anal cancers in males and females. The expanded indication broadens the rationale for use to prevent HPV-related cancers in both sexes and includes individuals ages 9 through 45 years.

The FDA granted the expanded indication under the accelerated approval licensure pathway. This pathway uses a surrogate endpoint for earlier approval of drugs or biologics that treat serious conditions and that fill an unmet medical need.

The FDA relied on effectiveness data used to support approval for prevention of HPV-related anogenital infection and disease as a surrogate to predict clinical benefit in prevention of HPV-related oropharyngeal infection and disease. It also used epidemiologic evidence to support that prevention of persistent oropharyngeal HPV infection is reasonably likely to predict prevention of HPV-related head and neck cancer.

As required with accelerated approval, a post-approval confirmatory study is underway to evaluate the safety and efficacy of Gardasil 9 vaccination for prevention of persistent oropharyngeal HPV infection. Analyses of the randomized, blinded, placebo-controlled trial will be driven by the number of oropharyngeal HPV-positive cases identified through polymerase chain reaction testing at six-month intervals. Once complete, the FDA will evaluate the study data to determine whether to grant traditional approval for this indication or remove the indication from the label.

HPV DNA has been detected in approximately one-quarter of all head and neck cancers (Joseph AW, et al.

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Otolaryngol Clin North Am. 2012;45:739-764), with HPV-16 present in approximately 90% of HPV-related oropharyngeal squamous cell carcinomas (Chaturvedi AK, et al. *J Clin Oncol*. 2011;29:4294-4301), followed by HPV types 33, 35, and 58 (Taberna M, et al. *Ann Oncol*. 2017;28:2386-2398).

HPV-related oropharyngeal squamous cell carcinoma is the most common HPV-related malignancy in the United States. Non-Hispanic White male nonsmokers under the age of 64 years account for a majority of patients diagnosed with HPV-positive oropharyngeal squamous cell carcinomas (Mahal BA, et al. *Cancer Epidemiology, Biomarkers & Prevention*. 2019).

Early detection is difficult because there are no easily identifiable pre-cancerous markers for HPV-related head and neck cancer, according to Joseph and colleagues.

Resources

- Information from the FDA on Gardasil 9
- Additional FDA Update columns