

FDA Strengthens Syncope Warning for Gardasil

BY MICHELE G. SULLIVAN

Patients who receive the Gardasil vaccine should sit or lie down in the office for at least 15 minutes after vaccination to prevent possible injury from falling during syncope, while being observed for paleness, sweating, dizziness, or other signs of a possible vasovagal reaction, the Food and Drug Administration recommended.

Because of continued reports of syncope and related traumatic injury, the FDA has requested that Merck and Co. Inc., manufacturer of the vaccine, add this information to the warnings and precautions section of the label.

"The addition of syncope to the [label] emphasizes that health care providers and consumers should be alert that fainting may occur following vaccination with Gardasil, sometimes resulting in falling and injuries," the FDA said in a public information statement. "These are preventable by having Gardasil recipients remain seated or lying down for 15 minutes following vaccination and closely watching them for the following warning signs and symptoms: paleness,

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sweating, dizziness, ringing in ears or vision changes, which generally occur before fainting."

Up to 40% of adolescent syncope associated with Gardasil is also accompanied by tonic-clonic seizure-like activity, the FDA said. "If an individual faints and especially if seizure-like activity occurs, the individual should be placed in a position, such as lying down, to help restore blood flow to the brain."

Syncope has been listed on the Gardasil label as a possible adverse event since October 2007, the statement said. However, the FDA's Vaccine Adverse Event Reporting System (VAERS) continues to receive reports of traumatic injuries related to fainting and falling after vaccination. In light of this, the agency decided to strengthen the label warning.

Fainting doesn't appear to be unique to Gardasil, the statement added. "Syncope has been reported after administration of other adolescent and adult vaccines. ... It can also occur with certain medications, after blood donation, or in response to pain."

The fact sheet did not give details of the injuries associated with all these events. However, 70 episodes of syncope in U.S. patients were reported in the May 2, 2008, issue of the Morbidity and Mortality Weekly Report (2008; 57:457-60). These events occurred from January 2005 to July 2007. The reports

noted that about 5% of the spells were considered serious; 38 occurred on the same day as vaccination and 37 required hospitalization.

As of May 1, 2009, there were 13,758 VAERS reports of adverse events following more than 24 million Gardasil vaccinations in the United States. Of these reports, 93% were considered non-serious and 7% serious. Nonserious adverse events include fainting, pain and

swelling at the injection site, headache, nausea, and fever.

However, the vaccine is still considered a safe and effective one, the FDA said in the public information statement. "Based on all of the information we have today, the Centers for Disease Control and Prevention continues to recommend Gardasil vaccination for the prevention of four types of human papillomavirus. As with all approved vaccines, CDC and FDA will


continue to closely monitor the safety of Gardasil. Any problems detected with this vaccine will be reported to health officials, health care providers, and the public, and needed action will be taken to ensure the public's health and safety." ■

Information regarding adverse events that are associated with Gardasil is available on the FDA's VAERS Web site (www.cdc.gov/vaccinesafety/vaers/gardasil.htm).

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Important Safety Information

Cardiovascular (CV) risk

- NSAIDs may cause an increased risk of serious CV thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk
- FLECTOR® Patch is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery

Gastrointestinal (GI) risk

- NSAIDs cause an increased risk of serious GI adverse events at any time during use and without warning symptoms including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. Elderly patients are at greater risk for serious GI events

FLECTOR® Patch is contraindicated in patients with known hypersensitivity to diclofenac. FLECTOR® Patch should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.

FLECTOR® Patch should not be applied to non-intact or damaged skin resulting from any etiology, e.g., exudative dermatitis, eczema, infected lesion, burns or wounds.

NSAIDs, including FLECTOR® Patch, can lead to new onset or worsening of hypertension, contributing to increased incidence of CV events. Fluid retention and edema have been observed in some patients taking NSAIDs. Use with caution in patients with hypertension, fluid retention or heart failure.

A patient with symptoms and/or signs of liver dysfunction, or with a history of an abnormal liver test, should be monitored for a more severe hepatic reaction and therapy stopped. Anemia is sometimes seen in patients receiving NSAIDs and platelet inhibition has been shown to prolong bleeding times.

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in maintaining renal perfusion. FLECTOR® Patch is not recommended in patients with advanced renal disease.

NSAIDs, including FLECTOR® Patch, can cause serious skin adverse events without warning such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.


Overall, the most common adverse events associated with FLECTOR® Patch were skin reactions (pruritus, dermatitis, burning, etc.) at the site of treatment and gastrointestinal disorders (nausea, dysgeusia, dyspepsia, etc.) and nervous system disorders (headache, paresthesia, somnolence, etc.).

In late pregnancy, as with other NSAIDs, FLECTOR® Patch should be avoided because it may cause premature closure of the ductus arteriosus. FLECTOR® Patch is in Pregnancy Category C. Safety and effectiveness in pediatric patients have not been established.


Please see Brief Summary of full Prescribing Information, including boxed warning, on adjacent page.

For more information, please visit www.FlectorPatch.com or www.KingPharm.com.

References: 1. Data on file. King Pharmaceuticals®, Inc. 2. Flector Patch [package insert]. Piscataway, NJ: Alpharma Pharmaceuticals LLC; 2008.



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