More Severe Illness a Concern

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said during the conference call.

According to Dr. Kolterman, from June 2005 to July 2008, the reporting rate for deaths and acute pancreatitis in patients taking exenatide was similar to the incidence rate in the general population. One million patients have taken the medication. The reporting rate for acute pancreatitis is 0.34 events per 1,000 patient-years of exposure.

In other words, for every 3,000 patients who have taken exenatide for 1 year, a single patient would have reported pancreatitis, he said, although he added that the reporting rate may not reflect the true incidence.

While the two deaths reported by the FDA appeared to be related to pancreatitis, the four additional deaths were not directly attributable to the inflammatory condition, said Dr. Kolterman. One patient died because of postoperative complications after gallbladder removal, and another from a leukemia relapse about 2 months after recovery from pancreatitis. The third patient died from postoperative intestinal bleeding after gallbladder removal. Dr. Kolterman said that the company was not able to get any information on the fourth death, despite multiple requests.

Acute pancreatitis was added as a precaution to exenatide's label in October 2007. At that time, the agency had received 30 reports of acute pancreatitis in patients taking the incretin mimetic for type 2 diabetes. Physicians were advised to stop exenatide injections if pancreatitis was suspected.

Now the FDA says that exenatide may also be linked to a more severe form of pancreatitis and again is advising physicians to discontinue the drug if the condition is suspected at all. "There are no signs or symptoms that distinguish acute hemorrhagic or necrotizing pancreatitis associated with Byetta from the less-severe form of pancreatitis," said the agency in a posting for health care professionals on its Web site.

In all six of the reported cases, the drug was stopped. All patients required hospitalization; two died, and four were recovering.

Dr. Zachary Bloomgarden, clinical professor in the division of endocrinology at Mount Sinai School of Medicine, in New York, was not too concerned about the reports. "The number of pancreatitis cases is quite a bit less than that expected in a population of persons at risk for pancreatitis," he said in an interview. "Indeed, the summary of the six severe pancreatitis cases shows clearly the doubtfulness of there being any relationship to the drug."

In the original FDA report of 30 cases, "there was one patient who had pancreatitis on Byetta and then developed it again after restarting the drug, so it must occur sometimes," he continued, "but we must realize that many drugs given to patients with diabetes have pancreatitis as an uncommon side effect, including diuretics and angiotensin-converting enzyme inhibitors."

The FDA said it is working with Amylin to "add stronger and more prominent warnings" about the risk of acute hemorrhagic and necrotizing pancreatitis to the drug's precautions section.

Physicians still can use exenatide, but it should not be started in a patient with a history of pancreatitis, said the FDA.

If pancreatitis is confirmed, the agency advises physicians to initiate appropriate treatment and monitor the patient until recovery. Exenatide should not be started again in that patient, the agency added.

Dr. Bloomgarden is on the speakers bureau for both Amylin and Lilly. ■

More information is available at www.fda.gov/medwatch/safety/2007/safety07.htm#Byetta.

FDA Rejects 'Approvable' Letter in Favor of 'Complete Response'

The Food and Drug Administration will no longer issue "approvable" or "not approvable" letters when a drug application is not approved, but will instead issue a "complete response" letter at the end of the review period, the agency has announced.

The change went into effect on Aug. 11 for all drug applications, regardless of when they were submitted.

"These new regulations will help the FDA adopt a more consistent and neutral way of conveying information to a company when we cannot approve a drug application in its present form," Dr. Janet Woodcock, director of the agency's Center for Drug Evaluation and Research, said in a statement.

Currently, when assessing new drug and generic drug applications, the FDA can respond to a sponsor in one of three types of letters: an "approval" letter, meaning the drug has met agency standards for safety and efficacy and can be marketed for sale in the United States; an "approvable" letter, which generally indicates that the drug can probably be approved at a later date provided that the applicant provides certain additional information or makes specified changes (such as to the labeling); or a "not approvable" letter, meaning the application has deficiencies generally requiring the submission of substantial additional data before approval.

A "complete response" letter, which will replace options 2 and 3, will be issued to inform the company that the review period for a drug is complete and that the application is not yet ready for approval, the statement said. The letter will describe specific deficiencies and, when possible, will outline recommended actions the applicant might take to prepare the application for approval. The way that the FDA communicates its decisions to approve an application—option 1—will not change.

The move brings the process for communication about drug licensing applications in line with that of biologics. The revision should not affect the overall time it takes the FDA to review new or generic drug applications, the agency said.

—Miriam E. Tucker

POLICY & PRACTICE

P4P Working, Says CMS

Providers that participated in a Medicare pay-for-performance demonstration program earned $16.7 million in incentive payments during the program's second year by improving the quality of care for patients with several chronic conditions, including heart failure, coronary artery disease, and diabetes, according to the Centers for Medicare and Medicaid Services. All 10 of the participating physician groups achieved benchmark or target performance on at least 25 out of 27 quality markers for patients with diabetes, coronary artery disease and heart failure. Five of the groups achieved benchmark quality performance on all 27 quality measures. The groups improved their performance by changing some of their office processes and investing in health information technology. "We are paying for better outcomes and we are getting higher quality and more value for the Medicare dollar," said Kerry Weems, CMS acting administrator. "And these results show that by working in collaboration with the physician groups on new and innovative ways to reimburse for high quality care, we are on the right track to find a better way to pay physicians." The demonstration project was originally scheduled to last 3 years but has since been extended to a fourth year.

Obesity as Dem. Platform Plank

The drafters of the Democratic Party Platform have included a section on obesity, marking what appears to be the first time the disorder has been mentioned in any national party platform. The document, which was approved by the full platform committee in early August, reads in part, "Our nation faces epidemics of obesity and chronic diseases as well as new threats like pandemic flu and bioterrorism. Yet despite all of this, less than 4 cents of every health care dollar is spent on prevention and public health. … We will ensure that Americans can benefit from healthy environments that allow them to pursue healthy choices. Additionally, as childhood obesity rates have more than doubled in the last 30 years, we will work to ensure healthy environments in our schools." Gary Foster, Ph.D., president of the Obesity Society, applauded the action. "We are pleased to see a major political party recognize the importance of obesity to the health of Americans and to the health care system overall," he said.

Feds Scrutinize Generic Maker

India's Ranbaxy Inc., 1 of the top 10 generic drug makers in the world, is being investigated by various arms of the federal government for allegedly introducing "adulterated or misbranded products" into the U.S. market. The company's auditor, Parexel Consulting, is also under scrutiny. According to a subpoena for documents filed in the U.S. District Court for the District of Maryland by the federal Department of Justice and the U.S. Attorney's Office in Maryland, Ranbaxy submitted false information to the Food and Drug Administration on sterility and bioequivalence, covered up violations of good manufacturing practice, and defrauded Medicare. Rep. John Dingell (D-Mich.) and Rep. Bart Stupak (D-Mich.) said that they will formally investigate the Ranbaxy situation. "If these allegations are true, Ranbaxy has imperiled the safety of Americans in a manner similar to the generic drug scandal we uncovered 20 years ago," said Rep. Dingell. "I would like to know whether FDA officials knew about these allegations and what, if any, action was taken."

Patients Cutting Health Care

To save money, many Americans are reducing the amount of medical care they receive, according to a survey of nearly 700 people by the National Association of Insurance Commissioners. Twenty-two percent of respondents to the July survey said they have reduced the number of times they see the doctor. In addition, 11% said they have cut back the number of prescription drugs they take, or reduced the dosage to make the prescription last longer. "Delaying medical treatment and regular physicals puts consumers at risk for potential health issues, and increases overall health insurance costs," said Kansas Insurance Commissioner Sandy Praeger, president of the NAIC. The vast majority of respondents did not change their health insurance policies; of the 5% who did make changes, 2% reduced coverage, 1% fell behind on payments, and 2% canceled their policies.

Specialists' Incomes Vary Widely

Incomes vary widely among the four medical specialties—geriatrics, hematology-oncology, nephrology, and rheumatology—that derive more than half of their revenues from government-run health insurance programs, a study showed. For example, geriatricians' incomes averaged $165,000 annually, versus $504,000 for hematologists, even though the two specialties require a similar amount of training, according to the study by Harvard Medical School researchers at Cambridge (Mass.) Health Alliance, published online in the Journal of General Internal Medicine. The study analyzes data from the national Medical Expenditure Panel Survey. The income disparity fuels the shortage of primary care physicians, said Dr. Karen Lasser, the study's lead author. "It's no surprise that there is a shortage of primary care doctors when debt-burdened medical students have much more lucrative career options," Dr. Lasser said in a statement. "What is surprising is that government fee schedules are behind much of this income discrepancy." In total, Medicare accounts for about 21% of payments to doctors, whereas Medicaid and other government programs account for 10%, according to the study.

—Joyce Frieden