Drug Monitor

ONLINE EDITION

A New Contender in the Diabetes Drug Arena

A new drug, liraglutide (Victoza; Novo Nordisk, Bagsvaerd, Denmark), has been approved by the FDA as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. As a glucagon-like peptide-1 (GLP-1) receptor agonist, liraglutide imitates endogenous human GLP-1 to encourage postmeal insulin production by the pancreas. It also delays gastric emptying.

In comparative trials with exenatide (a twice-daily GLP-1 receptor agonist approved by the FDA in April 2005), once-daily liraglutide was associated with significantly greater improvements in glycemic control and was better tolerated. Both drugs were associated with similar amounts of weight loss (–3.24 kg and –2.87 kg, respectively).

In five clinical trials involving nearly 4,000 people, the most common adverse effects reported with liraglutide therapy were headache, nausea, and diarrhea. The drug also has been associated with an increased risk of pancreatitis compared with other diabetes medications. As such, the FDA recommends caution when using the drug in patients with a history of pancreatitis. Treatment should be halted if any patient develops abdominal pain (with or without nausea and vomiting) while taking liraglutide, and the drug should be restarted only if blood tests rule out pancreatitis.

In animal studies involving mice and rats, liraglutide caused tumors of the thyroid gland, some of which were malignant—although the risk was greatest when a very high dose, eight times higher than that which is used in humans, was administered. Given the uncertainty about the risk of thyroid cancer in humans, the FDA does not recommend using liraglutide as first-line pharmacotherapy in patients whose diet and exercise interventions have failed to control type 2 diabetes, and the drug is contraindicated in patients at increased risk for medullary thyroid cancer.

The manufacturer will conduct postmarketing studies to evaluate the potential risks of thyroid cancer, cardiovascular problems, hypoglycemia, pancreatitis, and allergic reactions. Additionally, the drug was approved with a risk evaluation and mitigation strategy, which includes a medication guide and a communication plan to help providers and patients weigh the potential risks and benefits of therapy.

Sources: FDA press release. January 25, 2010.

Lancet. 2009;374(9683):39–47.

Diabetes Forecast news article. January 26, 2010. http://forecast.diabetes.org/magazine/only-online/fda-oks-diabetes-med.

Continued Aspirin After Gastric Bleeding—Weighing the Risks and Benefits

The usual protocol for treating a patient who develops peptic ulcer bleeding while receiving antiplatelet therapy for prevention or treatment of cardiovascular or cerebrovascular disease is to use an endoscopic device to stop the bleeding, offer antisecretory therapy (such as a histamine [H_2]-receptor antagonist or a proton pump inhibitor [PPI]), and discontinue the antiplatelet agent until the ulcer heals. Stopping the antiplatelet agent, however, may put the patient at greater risk for cardiovascular and cerebrovascular complications. To help determine whether aspirin therapy can be continued safely immediately following endoscopic treatment of peptic ulcer bleeding, researchers from the Institute of Digestive Disease, Chinese University of Hong Kong, Hong Kong conducted a parallel, randomized, placebo-controlled noninferiority trial.

For the study, they enrolled patients who presented to a tertiary endoscopy center with peptic ulcer bleeding between February 2003 and September 2006. All patients were receiving low dose aspirin therapy for treatment or prophylaxis of cardiovascular disease at the time of presentation, and all underwent endoscopic hemostasis within 24 hours of bleeding onset. After achieving hemostasis, 78 patients were assigned randomly to receive aspirin 80 mg/day, and 78 were assigned to receive placebo for eight weeks. All patients also received the PPI pantoprazole—in an initial 80-mg bolus injection, followed by an 8-mg/hour infusion for 72 hours, and an oral dose of 40 mg/day thereafter.

Within 30 days of endoscopic treatment, researchers confirmed 12 cases of recurrent bleeding: eight in the aspirin group and four in the placebo group (10.3% versus 5.4%, respectively). Despite the higher risk of recurrent bleeding, however, fewer aspirin recipients died (1.3%) than placebo recipients (12.9%) after 56 days. Most deaths in the placebo group were related to cardiovascular events. Furthermore, discontinuing aspirin therapy did not prevent the ulcer-related deaths of three patients who received placebo, despite use of a PPI. "The small number of deaths would restrict further interpretation of the results on mortality rates," the researchers say, "yet, the transfusion

requirements between the two treatments were almost identical, which implies that recurrent bleeding was relatively mild and did not affect clinical outcome of these patients."

The researchers conclude from their findings that the protective effect of aspirin seems to outweigh its potential gastrointestinal toxicity. They theorize that aspirin should be discontinued for three to five days after index bleeding but might be safely resumed after stabilization. This theory, however, needs further investigation.

Source: *Ann Intern Med.* 2010;152(1):1–9.