Insulin Pump Problems Are Mostly User Related

BY ELIZABETH MECHCATIE

GAITHERSBURG, MD. — Members of a Food and Drug Administration advisory panel agreed that although there are technological issues with insulin infusion pumps, these issues are outweighed by user-related issues.

The meeting of the FDA's General Hospital and Personal Use Devices Panel meeting was convened to discuss postmarketing reports of safety issues related to insulin infusion pumps in people with diabetes. These reports are from the FDA adverse event reporting database for devices. The panel was not asked to vote on any questions related to the topic.

Several endocrinologists on the panel stressed the importance of education for patients who receive an insulin pump in how well they do on insulin pump therapy, which is most commonly used in patients with type 1 diabetes.

Panelist Dr. Lamont Weide, an endocrinologist at Truman Medical Center, Kansas City, Mo., said that pump failure rates "seem to be very low" and that problems are usually patient driven.

Between Oct. 1, 2006, and Sept. 20, 2009, the FDA received 16,849 reports of adverse events associated with insulin pumps; most of the reports were provided by the manufacturers. At the meeting, the FDA presented information on the 16,797 reported events (including 310 deaths) for pumps made by the five top manufacturers.

The reports were far from complete: In most cases the problem with the pump was not described nor was the patient's age included; the cause of deaths associated with the pumps had not been thoroughly investigated or evaluated, according to the FDA. In approximately 20% of the reports, the problem with the device was listed as "unknown," and in 9% the problem was listed as "replace." These were the two most common explanations listed among the device problems reports. And as panelists pointed out, there is no denominator so event rates cannot be calculated.

The other most common problems listed were described as display of an error message on the device (almost 5%), failure to deliver (3%), and repair (3%). Less commonly reported problems included inaudible alarms, failure to prime or infuse, battery failure, or a blank screen.

The most commonly reported patient-related problems included hospitalization (21% of reports) and high blood glucose (almost 17% of reports). The other most commonly reported problems in patients included diabetic ketoacidosis (8%), hyperglycemia (8%), and low blood glucose (almost 5%).

The FDA advisory panel reviewed the almost 17,000 adverse event reports and agreed insulin pump failure rates were low, and that most problems were patient driven.

Of the 310 deaths, the most commonly listed causes were diabetic coma, hyperglycemia, hypoglycemia, diabetic ketoacidosis, and unresponsiveness. There were 29 deaths associated with a motor vehicle.

Safety issues included the scenario of a pump recall or pump dysfunction and the risk associated with a patient having to change the mode of insulin treatment to insulin injections while waiting for a new pump. In the short-term (within 48 hours), the time usually needed by a manufacturer to provide a patient with a new pump, panelists said the risks were minimal, provided that patients and their families had been educated about what to do in that situation and had nonexpired insulin available for injections. The long-term risks include poorer glucose control, since insulin pumps provide better glucose control and a lower risk of hypoglycemia than do multiple daily injections, according to panelists.

When asked about the relative risks associated with the continuing use of a defective pump, panelists said that a pump failure that results in overinfusion of insulin and the risk of severe hypoglycemia would be their biggest concern, particularly during the night, when patients who do not have a glucose sensor are not testing their blood glucose.

Advisory panel members have been screened for potential conflicts of interest related to the products under discussion prior to panel meetings. ■

In LEAD, Liraglutide Lowered HbA_{1c} With No Weight Gain, Hypoglycemia

BY SHERRY BOSCHERT

SAN FRANCISCO — The once-daily drug liraglutide may work better than other diabetes medications to help patients reach a combination of goals, a secondary analysis of data from pivotal liraglutide studies suggests.

The Food and Drug Administration approved liraglutide (Victoza) in January for adults with type 2 diabetes who fail first-line drug therapy, based on data from the pivotal Liraglutide Effect and Action in Diabetes (LEAD) studies. Liraglutide is an injectable human glucagonlike peptide–1 (GLP-1) analogue.

The LEAD trials were "truly heroic" in their number, breadth, and head-to-head comparisons with existing diabetes medications, and in most of those trials liraglutide was more effective at lowering hemoglobin A_{1c} levels, Dr. John B. Buse said at a meeting sponsored by the American Diabetes Association.

He reported on an analysis that combined data from the more than 3,900 patients in the LEAD studies to compare the effectiveness of various therapies at achieving a composite end point known among diabetologists as a "Zindex" (because the idea was first proposed by Dr. Bernard Zinman, professor of medicine at the University of Toronto).

The analysis assessed the proportion of patients achieving the Zindex of an HbA_{1c} level below 7% with no weight gain and no confirmed hypoglycemia by the end of the 26- to 52-week studies. A significantly greater proportion of patients on 1.8 mg/day of liraglutide (39%) achieved this Zindex, compared with those on twice-daily injections of the GLP-1 agonist exenatide (24%) or patients treated with glargine (15%), a sulfonylurea (8%), placebo (8%), or a thiazolidinedione (6%).

"An A_{1c} less than 7% without weight gain or hypoglycemia is something that's of substantial interest to patients and clinicians," said Dr. Buse, chief of endocrinology and director of the diabetes care center at the University of North Carolina at Chapel Hill.

A second analysis compared the data with a second composite of three goals identified as standards of care by the American Diabetes Association in 2008: an HbA_{1c} less than 7%, no weight gain, and a systolic blood pressure less than 130 mm Hg. The GLP-1 therapies have modest effects on BP and lipids, with potentially greater changes in BP on long-acting GLP-1 agonists, Dr. Buse noted.

Significantly more patients on 1.8 mg/day of liraglutide (25%) achieved this composite than did patients on exenatide (14%), a sulfonylurea (7%), glargine or placebo (5% each), or a thiazolidinedione (3%). ■

VITALS

Major Finding: A significantly greater proportion of patients on 1.8 mg/day of liraglutide (39%) achieved an HbA_{1c} level below 7% with no weight gain and no confirmed hypoglycemia by the end of the 26- to 52-week studies, compared with those on twice-daily injections of the GLP-1 agonist exenatide (24%) or patients treated with glargine (15%), a sulfonylurea (8%), placebo (8%), or a thiazolidinedione (6%).

Data Source: A secondary analysis that combined data from the more than 3,900 patients in the LEAD studies to compare the effectiveness of various therapies.

Disclosures: Novo Nordisk Inc., which markets liraglutide, sponsored the LEAD trials. Dr. Buse has been a consultant for or received research support from Novo Nordisk as well as Amylin Pharmaceuticals Inc. and Eli Lilly & Co., which together are marketing the long-acting version of Amylin's exenatide.

No Link Between TZDs, Diabetic Macular Edema

A study of nearly 3,500 patients shows no link between thiazolidinedione use and diabetic macular edema, but given case reports of such an association, the findings still must be interpreted with caution, researchers say.

The authors of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial Eye Substudy say the findings are reassuring yet inconclusive. "We cannot rule out the possibility of either a modest protective or deleterious association," wrote Walter T. Ambrosius, Ph.D., of Wake Forest University, Winston-Salem, N.C., and colleagues in the ACCORD Study Group. "A more definitive answer may be provided from the 4-year follow-up data, which will enable us to examine prospectively the relationship between thiazolidinedione exposure and [diabetic macular edema] incidence."

The Eye Substudy, which involved 3,473 participants from the ACCORD trial, is the largest study to examine the association between diabetic macular edema and thiazolidinedione (TZD) use, the authors noted. Subjects had a mean age of 62 years and were eligible if they had no previous laser photocoagulation or vitrectomy for diabetic retinopathy in either eye.

A total of 695 subjects (20%) had used TZDs, and 217 (6%) had diabetic macular edema. In the adjusted analysis, TZD use was not significantly associated with diabetic macular edema, nor were hemoglobin A_{1c}, duration of diabetes, gender, or ethnicity. Significant association was found between TZDs and both retinopathy and age (Arch. Ophthalmol. 2010;128:312-8).

The study was funded by the National Eye Institute and the National Heart, Lung, and Blood Institute. Dr. Gerstein has received honoraria and grants from GlaxoSmithKline. The University of North Carolina, Chapel Hill, has contracted with various pharmaceutical companies for coauthor Dr. John B. Buse's research or consulting on thiazolidinediones. Dr. Goff has received research funding from Merck and Co.

—Kate Johnson