



September 24, 2013

Data From Post-Hoc Analyses Presented at EASD Examine Safety Profile of Linagliptin in Adults with Type 2 Diabetes

Two pooled analyses of data from clinical trials in adults with type 2 diabetes, including the elderly with normal renal function to severe renal impairment, found similar incidence of adverse events for linagliptin compared with placebo

RIDGEFIELD, Conn. and INDIANAPOLIS, Sept. 24, 2013 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (Lilly; NYSE: LLY) today announced results from two post-hoc, pooled analyses of data from placebo-controlled clinical trials, which examined the safety of the dipeptidyl peptidase-4 (DPP-4) inhibitor linagliptin in adults with type 2 diabetes (T2D). These data were presented at the 49th Annual Meeting of the European Association for the Study of Diabetes (EASD).

Linagliptin, which is marketed as TRADJENTA[®] (linagliptin) tablets in the U.S., is a once-daily, 5 mg tablet used along with diet and exercise to improve glycemic control in adults with type 2 diabetes. Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis (increased ketones in the blood or urine). TRADJENTA has not been studied in patients with a history of pancreatitis, and it is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using TRADJENTA.

General safety analysis

Findings from a pooled, post-hoc analysis of safety data from 22 linagliptin clinical trials with 7,400 adults with T2D (4,810 received linagliptin, 2,590 received placebo) included the following¹:

- The hypoglycemic incidence rate for linagliptin compared with placebo was 11.5 percent vs. 14 percent, respectively
- Overall incidence of adverse events (AE) or serious adverse events (SAE) with linagliptin was similar to placebo (AE 56.5 percent versus 61.2 percent, and SAE 4.8 percent versus 6.3 percent, respectively)

"Drug safety is an important consideration in the selection of appropriate treatments for adults with type 2 diabetes, as different populations often may have drug contraindications and require dose adjustments to help manage their disease," said Prof. Nikolaus Marx, Professor of Medicine and Cardiology, University Hospital of Aachen, Germany. "The results presented today examine the safety profile of linagliptin."

Renal safety data in the elderly

Results from another post-hoc analysis² evaluated pooled data from seven randomized, placebo-controlled phase III clinical trials including 1,293 adults with T2D who were 65 years or older showed:

- Overall renal function, as assessed by estimated glomerular filtration rate (eGFR), was not significantly altered by treatment with linagliptin from baseline to week 24, compared with placebo (adjusted mean $\pm$ SE eGFR of -1.8 ± 0.7 mL/min for linagliptin vs. -1.1 ± 0.9 mL/min for placebo). The majority of patients in the linagliptin group had mild renal impairment with similar proportions of mild, moderate and severe renal impairment found in the placebo group.
- Renal and urinary AEs were experienced by 5.5 percent and 4.3 percent of linagliptin and placebo patients, respectively
- Incidence of investigator-defined hypoglycemia was lower in patients who received linagliptin compared with placebo (21.3 percent versus 24.7 percent), with most events occurring in trials that included a sulfonylurea or basal insulin as background therapy
- Acute renal failure occurred in 0.5 percent and 0.2 percent of linagliptin and placebo patients, respectively

"The results from these pooled analyses continued to demonstrate that linagliptin is a treatment option for a wide range of adults with type 2 diabetes, including the elderly and those with renal impairment," said Christophe Arbet-Engels, MD, PhD, vice president, metabolic clinical development and medical affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "These findings provide healthcare providers with additional information they may need to help manage the increasing number of adults with type 2 diabetes they work with every day."

The U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and several other regulatory authorities worldwide have approved linagliptin for the treatment of adults with T2D as monotherapy or in combination with metformin, metformin + sulfonylurea, and as add-on therapy to insulin. With linagliptin, no dose adjustment is required regardless of

declining renal function or hepatic impairment.^{3,4}

What are TRADJENTA tablets?

TRADJENTA is a prescription medicine that is used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

TRADJENTA is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

If you have had inflammation of the pancreas (pancreatitis) in the past, it is not known if you have a higher chance of getting pancreatitis while you take TRADJENTA.

Important Safety Information

What is the most important information I should know about TRADJENTA?

Serious side effects can happen to people taking TRADJENTA, including inflammation of the pancreas (pancreatitis), which may be severe and lead to death. Before you start taking TRADJENTA, tell your doctor if you have ever had pancreatitis, gallstones, a history of alcoholism, or high triglyceride levels.

Stop taking TRADJENTA and call your doctor right away if you have pain in your stomach area (abdomen) that is severe and will not go away. The pain may be felt going from your abdomen through to your back. The pain may happen with or without vomiting. These may be symptoms of pancreatitis.

Who should not take TRADJENTA?

Do not take TRADJENTA if you are allergic to linagliptin or any of the ingredients in TRADJENTA.

Symptoms of a serious allergic reaction to TRADJENTA may include rash, itching, flaking or peeling; raised red patches on your skin (hives); swelling of your face, lips, tongue and throat that may cause difficulty breathing or swallowing. If you have any symptoms of a serious allergic reaction, stop taking TRADJENTA and call your doctor right away.

What should I tell my doctor before using TRADJENTA?

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. TRADJENTA may affect the way other medicines work, and other medicines may affect how TRADJENTA works.

Especially tell your doctor if you take

- Other medicines that can lower your blood sugar, such as a sulfonylurea or insulin.
 - TRADJENTA may cause serious side effects, including low blood sugar (hypoglycemia). If you take TRADJENTA with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered while you take TRADJENTA.
 - Signs and symptoms of low blood sugar may include headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, or feeling jittery.
- rifampin (Rifadin[®], Rimactane[®], Rifater[®], Rifamate[®])*, an antibiotic that is used to treat tuberculosis.

Tell your doctor if you are pregnant or planning to become pregnant or are breastfeeding or plan to breastfeed.

What are the possible side effects of TRADJENTA?

The most common side effects of TRADJENTA include stuffy or runny nose, sore throat, cough and diarrhea.

You are encouraged to report negative side effects of prescription drugs to the U.S. FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more safety information, please see [Medication Guide and full Prescribing Information](#).

TJ CONS ISI 19JUNE2013

*The brands listed are trademarks of their respective owners and are not trademarks of Boehringer Ingelheim Pharmaceuticals, Inc. The makers of these brands are not affiliated with and do not endorse Boehringer Ingelheim Pharmaceuticals, Inc., or its products.

To learn more about TRADJENTA visit: www.TRADJENTA.com. For full prescribing information visit: <http://bidocs.boehringer->

ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/Pis/Tradjenta/Tradjenta.pdf or call Boehringer Ingelheim Pharmaceuticals, Inc. at 1-800-542-6257.

Please report any unexpected effects or product problems to the Boehringer Ingelheim Drug Information Unit by calling 1-800-542-6257.

About Diabetes

Approximately 25.8 million Americans⁵ and an estimated 371 million people worldwide⁶ have type 1 or type 2 diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases.⁵ Diabetes is a chronic condition that occurs when the body does not properly produce or use the hormone insulin.⁷ Diabetes was estimated to cost the U.S. \$245 billion in 2012.⁸

Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in the field of diabetes that centers on three compounds representing several of the largest diabetes treatment classes. This alliance leverages the companies' strengths as two of the world's leading pharmaceutical companies, combining Boehringer Ingelheim's solid track record of research-driven innovation and Lilly's innovative research, experience, and pioneering history in diabetes. By joining forces, the companies demonstrate commitment in the care of patients with diabetes and stand together to focus on patient needs. Find out more about the alliance at www.boehringer-ingelheim.com or www.lilly.com.

About Boehringer Ingelheim

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation (Ridgefield, CT) and a member of the Boehringer Ingelheim group of companies.

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 140 affiliates and more than 46,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel medications of high therapeutic value for human and veterinary medicine.

Social responsibility is a central element of Boehringer Ingelheim's culture. Involvement in social projects, caring for employees and their families, and providing equal opportunities for all employees form the foundation of the global operations. Mutual cooperation and respect, as well as environmental protection and sustainability are intrinsic factors in all of Boehringer Ingelheim's endeavors.

In 2012, Boehringer Ingelheim achieved net sales of about \$19.1 billion (14.7 billion euro). R&D expenditure in the business area Prescription Medicines corresponds to 22.5% of its net sales.

For more information please visit www.us.boehringer-ingelheim.com.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, IN, Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we work to meet the diverse needs of people with diabetes through research and collaboration, a broad and growing product portfolio and a continued commitment to providing real solutions—from medicines to support programs and more—to make lives better.

For more information, visit www.lillydiabetes.com.

P-LLY

TJ579214PR

This press release contains forward-looking statements about linagliptin tablets for the treatment of type 2 diabetes. It reflects Lilly's current beliefs; however, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that linagliptin will be commercially successful. For further discussion of these and other

risks and uncertainties, please see Lilly's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward- looking statements.

CONTACT:

Catherine London
Associate Director, Public Relations
Boehringer Ingelheim Pharmaceuticals, Inc.
Email: usnews@boehringer-ingelheim.com
Phone: (203) 798-4638

Tammy Hull
Communications Manager
Lilly Diabetes
Email: hullta@lilly.com
Phone: (317) 651-9116

References

1. Lehrke M et al. Safety and tolerability of linagliptin in 7,400 patients with Type 2 Diabetes: A pooled comprehensive analysis of prospective safety reporting in placebo-controlled studies. Poster No: 986. Presented at the European Association for the Study of Diabetes (EASD), September 23-27, Barcelona.
2. Patel S et al. Renal safety of linagliptin in elderly patients with Type 2 Diabetes: analysis of pooled patient data from seven Phase III clinical trials. Poster No: 926. Presented at the European Association for the Study of Diabetes (EASD), September 23-27, Barcelona.
3. Tradjenta® (linagliptin) tablets. Highlights of Prescribing Information. Initial US Approval: 2011.
4. EMA. Tradjenta® (linagliptin) tablets. EMA Summary of Product Characteristics. 2011.
5. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Center for Disease Control and Prevention, 2011.
6. International Diabetes Federation. Diabetes Atlas, 5th Edition: Fact Sheet. 2012.
7. International Diabetes Federation. IDF Diabetes Atlas, 5th Edition: What is Diabetes?
<http://www.idf.org/diabetesatlas/5e/what-is-diabetes>. Accessed on: July 18, 2013.
8. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013;36 (4):1033 1046.

(Logo: <http://photos.prnewswire.com/prnh/20031219/LLYLOGO>)

(Logo: <http://photos.prnewswire.com/prnh/20110825/DE57898LOGO>)

SOURCE Eli Lilly and Company; Boehringer Ingelheim

News Provided by Acquire Media