



May 29, 2012

## **Jentadueto® (linagliptin/metformin hydrochloride) tablets recommended for approval in the treatment of adults with type 2 diabetes in Europe**

### **Milestone reflects the commitment of Boehringer Ingelheim and Eli Lilly and Company in bringing new diabetes medicines to patients around the world who need them**

RIDGEFIELD, Conn. and INDIANAPOLIS, May 29, 2012 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today announced they have received a positive opinion from the European Medicines Agency's (EMA) medicinal committee recommending approval of Jentadueto® (linagliptin/metformin hydrochloride) tablets, a medicine combining the DPP-4 inhibitor, linagliptin (the active ingredient in Tradjenta® tablets, marketed under the trade name Trajenta® in Europe) and metformin in a single tablet taken twice daily.(1)

The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended the approval of JENTADUETO for use alongside diet and exercise to improve glycemic control in adults with type 2 diabetes who are inadequately controlled on their maximally tolerated dose of metformin alone or those already being treated with the combination of linagliptin and metformin. If approved by the European Commission, JENTADUETO will provide a new, single-tablet treatment option, taken twice daily, for adults with type 2 diabetes who need to improve control of their blood glucose.(2)

"The CHMP positive opinion for JENTADUETO marks another important regulatory milestone for the Boehringer Ingelheim and Eli Lilly and Company worldwide diabetes alliance, extending our commitment to bringing new medicines to those patients who need them," said Prof. Klaus Dugi, Corporate Senior Vice President Medicine, Boehringer Ingelheim. "Around the world, many people with type 2 diabetes require more than one treatment to adequately manage their blood sugar. By combining two important diabetes medicines in a single tablet, we believe that JENTADUETO will provide people with type 2 diabetes another way of improving control of their blood sugar."

JENTADUETO was approved by the U.S. Food and Drug Administration (FDA) in January 2012 as a prescription medicine used along with diet and exercise to improve glycemic control in adults with type 2 diabetes when treatment with both linagliptin and metformin is appropriate.(1) In clinical studies, initial combination therapy with JENTADUETO was superior to metformin monotherapy and to placebo in improving hemoglobin A1c (HbA1c or A1C) and fasting plasma glucose (FPG), with a similar safety and tolerability profile. No meaningful change in body weight was noted in any treatment group.(1)

At the maximum dose of 2.5 mg (linagliptin)/1000mg (metformin HCl) BID, JENTADUETO demonstrated placebo-corrected reductions in A1C levels of up to 1.7 percent (+0.1 percent for placebo and -1.6 percent for JENTADUETO).(1) A1C is measured in people with diabetes to provide an index of blood glucose control for the previous two to three months. JENTADUETO did not cause any meaningful change in body weight.(1) JENTADUETO can be used alone or in combination with a sulfonylurea, a commonly prescribed medication for type 2 diabetes. JENTADUETO is not for the treatment of type 1 diabetes or diabetic ketoacidosis (increased ketones in the blood or urine). It has not been studied in combination with insulin.(1) The JENTADUETO U.S. label contains a boxed warning for the risk of lactic acidosis, a serious metabolic complication that can occur due to metformin accumulation during treatment with JENTADUETO.(1)

Adverse reactions reported in greater than or equal to five percent of patients treated with JENTADUETO and more commonly than in patients treated with placebo included nasopharyngitis (the common cold) and diarrhea. Hypoglycemia was more commonly reported in patients treated with the combination of JENTADUETO and sulfonylurea compared with those treated with the combination of placebo, sulfonylurea and metformin. Pancreatitis was reported more often in patients randomized to linagliptin (1 per 538 person-years versus zero in 433 person-years for comparator).(1)

Linagliptin (5 mg, once daily) is marketed as Trajenta® across Europe and Canada, as Tradjenta® in the US, and Trazenta® in Japan, as well as in additional markets.

#### **About Diabetes**

Approximately 25.8 million Americans(3) and an estimated 366 million people worldwide(4) have type 1 and type 2 diabetes.

Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases.(3) Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin.(5)

#### **What is JENTADUETO?**

JENTADUETO is a prescription medicine that contains 2 diabetes medicines, linagliptin and metformin. JENTADUETO can be used along with diet and exercise to help control blood sugar in adults with type 2 diabetes when treatment with both linagliptin and metformin is appropriate.

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

It is not known if JENTADUETO is safe and effective when used with insulin.

## **IMPORTANT SAFETY INFORMATION**

### **What is the most important information I should know about JENTADUETO?**

#### **WARNING: RISK OF LACTIC ACIDOSIS**

Serious side effects can happen in people taking JENTADUETO. Metformin, one of the medicines in JENTADUETO, can cause a rare but serious condition called lactic acidosis (a build-up of lactic acid in the blood) that can cause death. Lactic acidosis is a medical emergency and must be treated in a hospital.

Stop taking JENTADUETO and call your doctor right away if you feel very weak or tired, have unusual muscle pain, have trouble breathing, are very sleepy, have sudden nausea and vomiting or diarrhea, feel cold, especially in your arms or legs, feel dizzy or lightheaded, or have a slow or irregular heartbeat, as these could be symptoms of lactic acidosis.

You have a higher chance of getting lactic acidosis with JENTADUETO if you have kidney problems, liver problems, congestive heart failure that requires medicines, drink alcohol very often, or drink a lot of alcohol in short-term "binge" drinking, get dehydrated (lose a large amount of body fluids), have certain x-ray tests with dyes or contrast agents that are injected into your body, have surgery, have a heart attack, severe infection, or stroke, and are 80 years of age or older and have not had your kidneys tested.

### **Who should not take JENTADUETO?**

#### **Do not take JENTADUETO if you:**

- have kidney problems
- have a condition called metabolic acidosis or diabetic ketoacidosis (increased ketones in the blood or urine)
- are allergic to linagliptin, metformin or any of the ingredients in JENTADUETO. Symptoms of any allergic reaction are rash, raised red patches on your skin (hives), and swelling of your face, lips, and throat that may cause difficulty breathing or swallowing. If you have any symptoms of a serious allergic reaction, stop taking JENTADUETO and call your doctor right away.

### **What should I tell my doctor before using JENTADUETO?**

#### **Before you take JENTADUETO, tell your doctor if you:**

- have kidney problems
- are going to get an injection of dye or contrast agents for an x-ray procedure. JENTADUETO will need to be stopped for a short time. Talk to your doctor about when you should stop JENTADUETO and when you should start JENTADUETO again.
- have liver problems
- have heart problems, including congestive heart failure
- drink alcohol very often, or drink a lot of alcohol in short term "binge" drinking
- have any other medical conditions
- are pregnant or planning to become pregnant. It is not known if JENTADUETO will harm your unborn baby. If you are pregnant, talk with your doctor about the best way to control your blood sugar while you are pregnant.
- are breast-feeding or plan to breast-feed. It is not known if JENTADUETO passes into your breast milk. Talk with your doctor about the best way to feed your baby if you take JENTADUETO.

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

Especially tell your doctor if you take:

- other medicines that can lower your blood sugar. JENTADUETO may cause serious side effects, including low blood

sugar (hypoglycemia), which may become worse in people who already take another medication to treat diabetes, such as a sulfonylurea or insulin. Tell your healthcare provider if you take other diabetes medicines. Your doctor may prescribe lower doses of the sulfonylurea medicine.

If you have symptoms of low blood sugar, you should check your blood sugar and treat it if it is low, then call your healthcare provider. Symptoms of low blood sugar include shaking, rapid heartbeat, hunger, headache, sweating, change in vision, and change in mood.

- rifampin (Rifadine®, Rimactane®, Rifater®, Rifamate®), an antibiotic that is used to treat tuberculosis.

Ask your doctor or pharmacist for a list of these medicines if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

### **What are the possible side effects of JENTADUETO tablets?**

The most common side effects of JENTADUETO include:

- stuffy or runny nose and sore throat
- diarrhea

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

### **Please see Important Safety Information including Boxed Warning about the Risk of Lactic Acidosis, and full Prescribing Information, including Patient Information for additional safety information.**

To learn more about JENTADUETO visit <http://www.JENTADUETO.com>. For full prescribing information visit <http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/Pis/Jentadueto/Jentadueto.pdf> or call Boehringer Ingelheim Pharmaceuticals, Inc. at 1-800-542-6257, or (TTY) 1-800-459-9906.

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

### **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).

It is not known if TRADJENTA is safe and effective when used with insulin.

### **Important Safety Information**

#### **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 are rash, raised red patches on your skin (hives), swelling of your face, lips, 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 taking TRADJENTA?**

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 medicine 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.

Also tell your doctor if you take rifampin (Rifadin®, Rimactane®, Rifater®, Rifamate®), an antibiotic that is used to treat tuberculosis.

TRADJENTA may affect the way other medicines work, and other medicines may affect how TRADJENTA works.

Tell your doctor if you are pregnant or planning to become pregnant or are breast-feeding or plan to breast-feed.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

### **What are the possible side effects of TRADJENTA?**

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

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

For more safety information, please see Patient Information and full Prescribing Information.

To learn more about TRADJENTA visit: [www.TRADJENTA.com](http://www.TRADJENTA.com). For full prescribing information visit: <http://bidocs.boehringer-ingenelheim.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.

### **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 four pipeline compounds representing several of the largest 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-ingenelheim.com](http://www.boehringer-ingenelheim.com) or [www.lilly.com](http://www.lilly.com).

### **About Boehringer Ingelheim Pharmaceuticals, Inc.**

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 145 affiliates and more than 44,000 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.

As a central element of its culture, Boehringer Ingelheim pledges to act socially responsible. 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 2011, Boehringer Ingelheim achieved net sales of about \$17.1 billion (13.2 billion euro). R&D expenditure in the business area Prescription Medicines corresponds to 23.5% of its net sales.

For more information, please visit <http://us.boehringer-ingenelheim.com> and follow us on Twitter at <http://twitter.com/boehringerus>.

### **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](http://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.

*This press release contains forward-looking statements about JENTADUETO 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 JENTADUETO will be approved for marketing or 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.*

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1. Jentaduetto® (linagliptin/metformin HCl) tablets. Highlights of Prescribing Information. Initial US Approval: 2012
2. Data on File
3. 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.
4. International Diabetes Federation. Diabetes Atlas, 5th Edition: Fact Sheet. 2011.
5. International Diabetes Federation. Diabetes Atlas, 5th Edition: What is Diabetes? <http://www.idf.org/diabetesatlas/5e/what-is-diabetes>. Accessed on: February 22, 2012.

SOURCE Eli Lilly and Company; Boehringer Ingelheim

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