



FDA approves Jentadueto™ (linagliptin/metformin hydrochloride) tablets for the treatment of adult patients with type 2 diabetes

New treatment combines DPP-4 inhibitor, linagliptin (the active ingredient in Tradjenta™ (linagliptin) tablets), and metformin in a single tablet, taken twice-daily, to lower blood sugar in adults with type 2 diabetes

RIDGEFIELD, Conn., and INDIANAPOLIS, Jan. 30, 2012 /PRNewswire/ -- Boehringer Ingelheim Pharmaceuticals, Inc. and Eli Lilly and Company (NYSE: LLY) today announced the U.S. Food and Drug Administration (FDA) has approved [Jentadueto™ \(linagliptin/metformin hydrochloride\) tablets](#), a new tablet combining the dipeptidyl peptidase-4 (DPP-4) inhibitor, linagliptin, and metformin. JENTADUETO provides a new, single-tablet treatment option, taken twice-daily, for patients who need to control their blood sugar. Linagliptin (5 mg, once-daily) is marketed in the U.S. as [Tradjenta™ \(linagliptin\) tablets](#)

JENTADUETO is a prescription medication 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. At the maximum dose, JENTADUETO demonstrated placebo-corrected reductions in hemoglobin A(1c) (HbA(1c) or A1C) levels of up to 1.7 percent (+0.1 percent for placebo and -1.6 percent for JENTADUETO). A1C is measured in people with diabetes to provide an index of blood sugar control for the previous two to three months. JENTADUETO did not cause any meaningful change in body weight. 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. The JENTADUETO 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.

"Most people with type 2 diabetes require more than one medication to help lower their blood sugar, due to the complex nature of type 2 diabetes," said Lance Sloan, MD, Texas Institute for Kidney and Endocrine Disorders. "The approval of JENTADUETO is exciting because it combines two diabetes medications in a single tablet, making it a good option for people who need an additional medication, and for whom both linagliptin and metformin is appropriate."

JENTADUETO Clinical Trials

In a 24-week, randomized, double-blind, placebo-controlled factorial study evaluating 791 adult patients with type 2 diabetes and inadequate glycemic control with diet and exercise, linagliptin plus metformin demonstrated the following:

	Placebo	5 mg linagliptin once-daily	500 mg metformin twice-daily	2.5 mg linagliptin/ 500 mg metformin twice-daily	1,000 mg metformin twice-daily	2.5 mg linagliptin/ 1,000 mg metformin twice-daily
A1C (%)						
Change from baseline (adjusted mean)	+0.1	-0.5	-0.6	-1.2	-1.1	-1.6
Difference from placebo (adjusted mean)	--	-0.6	-0.8	-1.3	-1.2	-1.7
*FPG (mg/dL)						
Change from baseline (adjusted mean)	+10	-9	-16	-33	-32	-49
Difference from placebo (adjusted mean)	--	-19	-26	-43	-42	-60

*Fasting plasma glucose (FPG) is used to determine glucose levels in a fasting state (usually upon waking in the morning).

JENTADUETO was approved based on clinical trials that evaluated linagliptin and metformin as separate tablets. Bioequivalence of JENTADUETO was demonstrated with co-administered linagliptin and metformin tablets in healthy subjects.

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 (22.9 percent versus 14.8 percent, respectively). Pancreatitis was reported more often in patients randomized to linagliptin (1 per 538 person years versus zero in 433 person years for comparator).

"We are proud to bring this important, new, single-tablet treatment option, taken twice-daily, to the millions of people currently living with type 2 diabetes," said David Pass, PharmD, vice president, cardiovascular and metabolic disorders marketing, Boehringer Ingelheim Pharmaceuticals, Inc. "We are hopeful that JENTADUETO, the newest member of the growing family of products from the Boehringer Ingelheim and Lilly diabetes alliance, may help people living with blood sugar levels that are not controlled."

The FDA approval of JENTADUETO marks the second U.S. approval since the formation of the Boehringer Ingelheim and Lilly worldwide diabetes alliance in January 2011. The alliance leverages the collective scientific expertise and business capabilities of two leading research-driven pharmaceutical companies to address patient needs arising from the growing global diabetes epidemic.

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 www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see Important Safety Information for 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://us.boehringer-ingelheim.com/content/dam/internet/opu/us_EN/documents/products/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 breastfeeding or plan to breastfeed.

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 or call 1-800-FDA-1088.

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

Replacement Card

If you are already enrolled in the TRADJENTA Savings Card Program and need a replacement card please call the TRADJENTA Savings Card Program at 1-877-512-4246. Our customer service representatives are available to assist you.

To learn more about TRADJENTA and for full prescribing information visit: <http://www.TRADJENTA.com> 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 JENTADUETO

JENTADUETO combines two medicines that demonstrated improvements in blood sugar control: the DPP-4 inhibitor, linagliptin, and metformin. Linagliptin (5 mg, once-daily) is marketed in the U.S. as TRADJENTA.

TRADJENTA has demonstrated significant reductions in A1C when used as monotherapy and in combination with metformin, sulfonylurea and pioglitazone. Metformin is a commonly used antihyperglycemic medication that improves glucose tolerance by lowering both basal and postprandial plasma glucose.

About Diabetes

Approximately 25.8 million Americans⁽¹⁾ and an estimated 366 million people⁽²⁾ worldwide have diabetes, according to 2010 data from CDC and 2011 data from IDF. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases.⁽¹⁾ Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin.⁽³⁾

About 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 <http://www.boehringer-ingelheim.com> or <http://www.lilly.com>.

About Boehringer Ingelheim Pharmaceuticals, Inc.

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 145 affiliates and more than 42,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products 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 2010, Boehringer Ingelheim posted net sales of approximately \$16.7 billion (about 12.6 billion euro) while spending almost 24 percent of net sales in its largest business segment, Prescription Medicines, on research and development.

For more information, please visit <http://us.boehringer-ingelheim.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 <http://www.lilly.com>.

About Lilly Diabetes

For more than 85 years, Lilly has been a worldwide leader in pioneering industry-leading solutions to support people living with and treating diabetes. Lilly introduced the world's first commercial insulin in 1923, and remains at the forefront of medical and delivery device innovation to manage diabetes. Lilly is also committed to providing solutions beyond therapy — practical tools, education, and support programs to help overcome barriers to success along the diabetes journey. At Lilly, the journeys of each person living with or treating diabetes inspire ours. For more information, visit <http://www.lillydiabetes.com>.

This press release contains forward-looking statements about JENTADUETO and TRADJENTA 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 or TRADJENTA 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) Centers for Disease Control and Prevention. National Diabetes Fact Sheet 2011. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed on: January 23, 2012.

(2) International Diabetes Federation. Diabetes Atlas Fact Sheet. 5th edn. Brussels: International Diabetes Federation, 2011.

(3) International Diabetes Federation. Diabetes Atlas. 3rd edn. Brussels: International Diabetes Federation, 2006.

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