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U.S. FDA approves Synjardy® XR (empagliflozin/metformin hydrochloride extended-release) tablets for adults with type 2 diabetes

New once-a-day formulation indicated to improve blood sugar when used along with diet and exercise

RIDGEFIELD, Conn. and INDIANAPOLIS, Dec. 12, 2016 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has approved Synjardy® XR (empagliflozin and metformin hydrochloride extended-release) tablets for adults with type 2 diabetes. When used along with diet and exercise, SYNJARDY XR is indicated to improve blood sugar in adults with type 2 diabetes when both empagliflozin and metformin can be taken. It is marketed by Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY).

SYNJARDY XR is a combination of empagliflozin and metformin — two medicines with complementary mechanisms of action — to help improve blood glucose in adults with type 2 diabetes. Empagliflozin, a sodium-glucose co-transporter 2 inhibitor, removes excess glucose through the urine by blocking glucose re-absorption in the kidney. SYNJARDY XR is the fourth FDA-approved treatment that contains empagliflozin. Metformin, a commonly prescribed initial treatment for type 2 diabetes, lowers glucose production by the liver and its absorption in the intestine.

"Adults with type 2 diabetes often take multiple medications, sometimes more than once a day, to manage their condition," said Paul Fonteyne, president and CEO, Boehringer Ingelheim Pharmaceuticals, Inc. "With SYNJARDY XR, the eighth FDA-approved treatment to emerge from our partnership with Lilly, adults with type 2 diabetes now have another convenient daily option to help them reach their glycemic goals, whether they are already being treated or are just at the beginning of their treatment."

The FDA approval of SYNJARDY XR is based on results from multiple clinical trials examining the co-administration of empagliflozin and metformin, alone or in combination with sulfonylurea, in the treatment of adults with type 2 diabetes. SYNJARDY XR is not for the treatment of type 1 diabetes or diabetic ketoacidosis.

SYNJARDY XR can cause serious side effects, including lactic acidosis (a buildup of lactic acid in the blood). Metformin, one of the medicines in SYNJARDY XR, can cause lactic acidosis, a rare, but serious condition that can cause death. Lactic acidosis is a medical emergency and must be treated in a hospital. SYNJARDY XR can cause dehydration, low blood pressure and increased ketones in the blood (ketoacidosis).

About Diabetes

Approximately 29 million Americans and an estimated 415 million people worldwide have diabetes, and nearly 28 percent of Americans with diabetes—totaling 8 million people—are undiagnosed. In the U.S., approximately 12 percent of those aged 20 and older have diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diagnosed adult diabetes cases in the U.S. Diabetes is a chronic condition that occurs when the body does not properly produce or use the hormone insulin.

What is SYNJARDY XR? (www.synjardy.com)

SYNJARDY XR is a prescription medicine that contains 2 diabetes medicines, empagliflozin and metformin. SYNJARDY XR can be used along with diet and exercise to improve blood sugar in adults with type 2 diabetes when both metformin and empagliflozin can be taken.

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

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about SYNJARDY XR?

SYNJARDY XR can cause serious side effects, including Lactic Acidosis (a build-up of lactic acid in the

blood). Metformin, one of the medicines in SYNJARDY XR, can cause lactic acidosis, a rare, but serious condition that can cause death. Lactic acidosis is a medical emergency and must be treated in a hospital.

Call your doctor right away if you get any of the following symptoms of lactic acidosis: cold in your hands or feet; feel dizzy or lightheaded; slow or irregular heartbeat; feel very weak or tired; have unusual muscle pain; have trouble breathing; feel sleepy or drowsy; have stomach pains, nausea, or vomiting.

You have a higher chance of getting lactic acidosis with SYNJARDY XR if you: have moderate to severe kidney problems or your kidneys are affected by injectable dyes used for certain x-ray tests; have liver problems; drink alcohol very often, or drink a lot of alcohol in the short-term ("binge" drinking); get dehydrated (lose a large amount of body fluids); have surgery; have a heart attack, severe infection, or stroke.

Who should not take SYNJARDY XR?

Do not take SYNJARDY XR if you:

- | have moderate to severe kidney problems or are on dialysis
- | have a condition called metabolic acidosis or diabetic ketoacidosis (increased ketones in the blood or urine)
- | are allergic to empagliflozin, metformin, or any of the ingredients in SYNJARDY XR. Symptoms of serious allergic reactions to SYNJARDY XR may include skin rash, raised red patches on your skin (hives), swelling of the face, lips, tongue, and throat that may cause difficulty breathing or swallowing. If you have any of these symptoms, stop taking SYNJARDY XR and contact your doctor or go to the nearest emergency room right away

What should I tell my doctor before using SYNJARDY XR?

Tell your doctor about all of your medical conditions, including if you:

- | have moderate to severe kidney problems. Your doctor may do blood tests to check your kidneys before and during treatment with SYNJARDY XR
- | have liver problems
- | have a history of urinary tract infection or problems with urination
- | have heart problems, including congestive heart failure
- | are going to have surgery
- | are eating less due to illness, surgery, or a change in your diet
- | have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas
- | drink alcohol very often, or drink a lot of alcohol in the short-term ("binge" drinking)
- | are going to get an injection of dye or contrast agents for an x-ray procedure. SYNJARDY XR may need to be stopped for a short time. Talk to your doctor about when you should stop SYNJARDY XR and when you should start it again
- | have type 1 diabetes. SYNJARDY XR should not be used in people with type 1 diabetes
- | are pregnant or planning to become pregnant. SYNJARDY XR may harm your unborn baby. Tell your doctor right away if you become pregnant while taking SYNJARDY XR
- | are a premenopausal woman (before the "change of life"), who does not have periods regularly or at all. Talk to your doctor about birth control choices while taking SYNJARDY XR as it may increase your chances of becoming pregnant
- | are breastfeeding or plan to breastfeed. SYNJARDY XR may pass into your breast milk and may harm your baby. Do not breastfeed while taking SYNJARDY XR.

Tell your doctor about all the medicines you take including prescription or over-the-counter medicines, vitamins, or herbal supplements.

What are the possible side effects of SYNJARDY XR?

SYNJARDY XR may cause serious side effects including:

Dehydration. SYNJARDY XR can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up. You may be at higher risk of dehydration if you have low blood pressure, kidney problems, are 65 years of age or older, on a low salt diet, or take medicines to lower your blood pressure, including water pills (diuretics).

Ketoacidosis (increased ketones in your blood or urine). Ketoacidosis is a serious condition and may need to be treated in the hospital. Ketoacidosis may lead to death. Ketoacidosis occurs in people with type 1 diabetes and can also occur in people with type 2 diabetes taking SYNJARDY XR, even if blood sugar is less than 250 mg/dL. **Stop taking**

SYNJARDY XR and call your doctor right away if you get any of the following symptoms, and, if possible, check for ketones in your urine:

- | nausea
- | vomiting
- | stomach-area (abdominal) pain
- | tiredness
- | trouble breathing

Kidney problems. Sudden kidney injury has happened to people taking SYNJARDY XR. Talk to your doctor right away if you reduce the amount you eat or drink, or if you lose liquids; for example, from vomiting, diarrhea, or being in the sun too long.

Serious urinary tract infections. Serious urinary tract infections can occur in people taking SYNJARDY XR and may lead to hospitalization. Tell your doctor if you have symptoms of a urinary tract infection, such as a burning feeling when passing urine, a need to urinate often or right away, pain in the lower part of your stomach or pelvis, or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.

Low blood sugar (hypoglycemia). If you take SYNJARDY XR with another medicine that can cause low blood sugar, such as a 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. Symptoms of low blood sugar may include headache, drowsiness, weakness, irritability, hunger, fast heartbeat, confusion, shaking or feeling jittery, dizziness, or sweating.

Vaginal yeast infection. Women who take SYNJARDY XR may get vaginal yeast infections. Talk to your doctor if you experience vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), and/or vaginal itching.

Yeast infection of the penis. Men who take SYNJARDY XR may get a yeast infection of the skin around the penis, especially uncircumcised males and those with chronic infections. Talk to your doctor if you experience redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and/or pain in the skin around penis.

Low vitamin B12 (vitamin B12 deficiency). Using metformin for long periods of time may cause a decrease in the amount of vitamin B12 in your blood, especially if you have had low vitamin B12 blood levels before. Your doctor may do blood tests to check your vitamin B12 levels.

Increased fats in your blood (cholesterol).

Other common side effects of SYNJARDY XR include diarrhea, nausea, vomiting, gas, stomach pain, indigestion, weakness, and headache.

These are not all the possible side effects of SYNJARDY XR. For more information, ask your doctor or pharmacist.

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 information, please see [Prescribing Information](#) and [Medication Guide](#).

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Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in diabetes that centers on compounds representing several of the largest diabetes treatment classes. This alliance leverages the strengths of two of the world's leading pharmaceutical companies. 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.

Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally with 145 affiliates and more than 47,000 employees. Since its founding in 1885, the family-

owned company has been committed to researching, developing, manufacturing and marketing novel treatments for human and veterinary medicine.

Boehringer Ingelheim is committed to improving lives and providing valuable services and support to patients and families. Our employees create and engage in programs that strengthen our communities. To learn more about how we make more health for more people, visit our [Corporate Social Responsibility Report](#).

In 2015, Boehringer Ingelheim achieved net sales of about \$15.8 billion (14.8 billion euros). R&D expenditure corresponds to 20.3 percent of its net sales.

For more information please visit www.boehringer-ingelheim.us/, or follow us on Twitter @BoehringerUS.

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 are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research and collaboration, a wide range of therapies and a continued determination to provide real solutions—from medicines to support programs and more—we strive to make life better for all those affected by diabetes around the world. For more information, visit www.lillydiabetes.com.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/newsroom/social-channels.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about SYNJARDY XR as a treatment of adults with type 2 diabetes, and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that SYNJARDY XR will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

Synjardy XR[®] is a registered trademark of Boehringer Ingelheim.

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