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## **U.S. FDA expands indication for type 2 diabetes treatment Synjardy® (empagliflozin/metformin hydrochloride) to include treatment-naïve adults**

RIDGEFIELD, Conn., and INDIANAPOLIS, July 19, 2016 /PRNewswire/ -- The U.S. Food and Drug Administration has approved an expanded indication for Synjardy® (empagliflozin and metformin hydrochloride) tablets to include treatment-naïve adults with type 2 diabetes (T2D). SYNJARDY, from Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY), is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D when treatment with both empagliflozin and metformin is appropriate.

SYNJARDY is a combination of empagliflozin (Jardiance®) and metformin — two medicines with complementary mechanisms of action — to help control blood glucose in adults with T2D. Empagliflozin, a sodium glucose co-transporter-2 inhibitor, removes excess glucose through the urine by blocking glucose re-absorption in the kidney. Metformin, a commonly prescribed initial treatment for T2D, lowers glucose production by the liver and its absorption in the intestine.

"Type 2 diabetes is a complex condition, which often requires that people take more than one treatment to manage their blood sugar," said Paul Fonteyne, president and CEO, Boehringer Ingelheim Pharmaceuticals, Inc. "The expanded indication for SYNJARDY further validates the potential of this combination therapy to help adults with type 2 diabetes who are not at goal, including those already being treated and, now, those at the beginning of their treatment journey."

The SYNJARDY label was updated to include results from a phase III, double-blind, randomized, active-controlled study that evaluated the efficacy and safety of empagliflozin in combination with metformin as initial therapy compared with the individual components. In the study, at 24 weeks, the combination of empagliflozin 10 mg or 25 mg with metformin 1000 mg or 2000 mg resulted in significant reductions in A1C (a measure of average blood glucose over the past two to three months) compared with the corresponding dose of either component alone.

SYNJARDY can cause serious side effects, including Lactic Acidosis (a buildup of lactic acid in the blood). Metformin, one of the medicines in SYNJARDY, 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 is not for the treatment of type 1 diabetes or diabetic 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. T2D 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 either does not properly produce, or use, the hormone insulin.

### **What is SYNJARDY?**

SYNJARDY is a prescription medicine that contains 2 diabetes medicines, empagliflozin (JARDIANCE) and metformin. SYNJARDY can be used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

SYNJARDY 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?**

**SYNJARDY can cause serious side effects, including Lactic Acidosis (a build-up of lactic acid in the blood). Metformin, one of the medicines in SYNJARDY, 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 if you: have moderate to severe kidney problems or your kidneys are affected by certain x-ray tests that use injectable dye; 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?**

#### **Do not take SYNJARDY 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 (JARDIANCE), metformin, or any of the ingredients in SYNJARDY. Symptoms of serious allergic reactions to SYNJARDY 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 and contact your doctor or go to the nearest emergency room right away

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

#### **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
- | 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 may need to be stopped for a short time. Talk to your doctor about when you should stop SYNJARDY and when you should start SYNJARDY again
- | have type 1 diabetes. SYNJARDY should not be used in people with type 1 diabetes
- | are pregnant or planning to become pregnant. SYNJARDY may harm your unborn baby. Tell your doctor right away if you become pregnant while taking SYNJARDY
- | 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 as it may increase your chances of becoming pregnant
- | are breastfeeding or plan to breastfeed. SYNJARDY may pass into your breast milk and may harm your baby. Do not breastfeed while taking SYNJARDY.

**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?**

#### **SYNJARDY may cause serious side effects including:**

**Dehydration.** SYNJARDY 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, even if blood sugar is less than 250 mg/dL. **Stop taking SYNJARDY 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

**Serious urinary tract infections.** Serious urinary tract infections can occur in people taking SYNJARDY 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.

**Kidney problems.** SYNJARDY can cause kidney problems, especially in people 75 years of age or older and people who already have kidney problems.

**Low blood sugar (hypoglycemia).** If you take SYNJARDY 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 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 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).**

**The most common side effects of SYNJARDY** include stuffy or runny nose and sore throat, urinary tract infections, female genital infections, diarrhea, headache, nausea, and vomiting.

These are not all the possible side effects of SYNJARDY. 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](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.**

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

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## **What is JARDIANCE?**

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

**JARDIANCE can cause serious side effects, including:**

- | **Dehydration.** JARDIANCE 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 a higher risk of dehydration if you:

- | have low blood pressure

- | take medicines to lower your blood pressure including water pills (diuretics)
  - | are on a low salt diet
  - | have kidney problems
  - | are 65 years of age or older.
- | **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 JARDIANCE, even if blood sugar is less than 250 mg/dL. **Stop taking JARDIANCE 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
- | **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE 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.
- | **Vaginal yeast infection.** Women who take JARDIANCE 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 JARDIANCE 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.

### Who should not take JARDIANCE?

**Do not take** JARDIANCE if you are allergic to empagliflozin or any of the ingredients in JARDIANCE. Symptoms of serious allergic reactions to JARDIANCE 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 JARDIANCE and contact your doctor or go to the nearest emergency room right away.

**Do not take** JARDIANCE if you have severe kidney problems or are on dialysis.

### What should I tell my doctor before using JARDIANCE?

#### Tell your doctor if you:

- | have kidney problems. Your doctor may do blood tests to check your kidneys before and during your treatment with JARDIANCE
- | have liver problems
- | have a history of urinary tract infections or problems with urination
- | 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)
- | have any other medical conditions
- | are pregnant or planning to become pregnant. It is unknown if JARDIANCE will harm your unborn baby
- | are breastfeeding, or plan to breastfeed. It is unknown if JARDIANCE passes into your breast milk.

**Tell your doctor about all the medicines you take** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take water pills (diuretics) or medicines that can lower your blood sugar such as insulin.

## What are other possible side effects of JARDIANCE?

- | **Low blood sugar** (hypoglycemia): if you take JARDIANCE with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered. Symptoms of low blood sugar may include:
  - | Headache
  - | Drowsiness
  - | Weakness
  - | Dizziness
  - | Confusion
  - | Irritability
  - | Hunger
  - | Fast heart beat
  - | Sweating
  - | Shaking or feeling jittery
- | **Kidney Problems**, especially in people 75 years of age or older and people who already have kidney problems
- | **Increased fats in your blood (cholesterol).**

The most common side effects of JARDIANCE include urinary tract infections, and yeast infections in females.

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 information, please see [full Prescribing Information, including Patient Information](#).

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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](http://www.boehringer-ingelheim.com) or [www.lilly.com](http://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 dollars (14.8 billion euros). R&D expenditure corresponds to 20.3 percent of its net sales.

For more information please visit [www.us.boehringer-ingelheim.com](http://www.us.boehringer-ingelheim.com), 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 broad and growing product portfolio 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](http://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](http://www.lilly.com) and [newsroom.lilly.com/social-channels](http://newsroom.lilly.com/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 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 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.*

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