



August 27, 2015

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

SYNJARDY approval was based on multiple clinical trials showing reductions in blood glucose versus placebo

RIDGEFIELD, Conn. and INDIANAPOLIS, Aug. 27, 2015 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has approved Synjardy® (empagliflozin and metformin hydrochloride) tablets, from Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI) and Eli Lilly and Company (NYSE: LLY), for the treatment of adults with type 2 diabetes (T2D). SYNJARDY is the third product containing empagliflozin to be approved by the FDA, following Jardiance® (empagliflozin) and Glyxambi® (empagliflozin/linagliptin).

SYNJARDY is a combination of empagliflozin and metformin — two medicines with complementary mechanisms of action — to help control blood glucose in people with T2D. Empagliflozin, a sodium glucose co-transporter-2 (SGLT2) 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.

"SYNJARDY is now the fifth FDA-approved medicine to emerge from the BI-Lilly Diabetes alliance pipeline in the last four years," said Paul Fonteyne, president and CEO, BIPI. "No two people with diabetes are alike, and every experience is different. Our alliance is proud to offer a diverse portfolio of treatments that can help patients throughout their diabetes journey."

SYNJARDY is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D who are not adequately controlled on a regimen containing empagliflozin or metformin, or in patients already being treated with empagliflozin and metformin. SYNJARDY is not for the treatment of type 1 diabetes or diabetic ketoacidosis.

The SYNJARDY 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 SYNJARDY.

The FDA approval of SYNJARDY 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 T2D.

SYNJARDY was also recently approved by the European Medicines Agency in May 2015.

About Diabetes

Approximately 29 million Americans and an estimated 387 million people worldwide have type 1 or type 2 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 and metformin. SYNJARDY can be used along with diet and exercise to improve blood sugar in adults with type 2 diabetes who have already been treated with either empagliflozin or metformin and their blood sugar is not controlled well enough, or who are currently taking both empagliflozin and metformin as separate medicines.

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?

WARNING: RISK OF LACTIC ACIDOSIS

Serious side effects can happen in people taking SYNJARDY. Metformin, one of the medicines in SYNJARDY, 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 SYNJARDY and call your doctor right away if you get any of the following symptoms of lactic acidosis: you feel very weak or tired; have unusual muscle pain; have trouble breathing; are very sleepy or sleep longer than usual; have sudden stomach pains, 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 SYNJARDY 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, are 80 years of age or older and have not had your kidneys tested.

Who should not take SYNJARDY?

Do not take SYNJARDY if you:

- have 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. 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 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
- drink alcohol very often, or drink a lot of alcohol in short-term "binge" drinking
- are going to get an injection of dye or contrast agents for an x-ray procedure. SYNJARDY will 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 is not for people with type 1 diabetes
- are pregnant or planning to become pregnant. It is not known if SYNJARDY will harm your unborn baby. Tell your doctor right away if you become pregnant during treatment with SYNJARDY
- are breastfeeding or plan to breastfeed. It is not known if SYNJARDY passes into your breast milk

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, are on a low salt diet, or take medicines to lower your blood pressure, including water pills (diuretics).
- **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.
- **Kidney problems.** SYNJARDY can cause kidney problems, especially in people 75 years of age or older and people who already have kidney problems.
- **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.
- **Urinary tract infection.** Tell your doctor if you have any signs and symptoms of a urinary tract infection that may include a burning feeling when passing urine, urine that looks cloudy, pain in the pelvis, or back pain.
 - **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.com 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 once-daily pill taken in the morning, used along with diet and exercise, to lower blood sugar (A1C) 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.

- 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 the 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
- 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
 - Confusion
 - Sweating
 - Drowsiness
 - Irritability
 - Shaking or feeling jittery
 - Weakness
 - Hunger
 - Dizziness
 - Fast heart beat
- **Kidney Problems**, especially in people 75 years of age or older and people who already have kidney problems.
- **Urinary Tract Infection**: symptoms may include burning feeling when passing urine, pain in the pelvis or back, or urine that looks cloudy.
- **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 or call 1-800-FDA-1088.

For more information, please see [Full Prescribing Information, including Patient Information](#).

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What is GLYXAMBI?

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

IMPORTANT SAFETY INFORMATION

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

Serious side effects can happen to people taking GLYXAMBI, including:

- **Inflammation of the pancreas** (pancreatitis), which may be severe and lead to death. Before you start taking GLYXAMBI, tell your doctor if you have ever had pancreatitis, gallstones, a history of alcoholism, or high triglyceride levels.

Stop taking GLYXAMBI 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 to your back. The pain may happen with or without vomiting. These may be symptoms of pancreatitis.

- **Dehydration.** GLYXAMBI 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, take medicines to lower your blood pressure, including water pills (diuretics), are on a low salt diet, have kidney problems, or are 65 years of age or older.
- **Vaginal yeast infection.** Women who take GLYXAMBI 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 GLYXAMBI 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 GLYXAMBI?

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

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

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

What should I tell my doctor before using GLYXAMBI?

Tell your doctor if you:

- have kidney problems. Your doctor may do blood tests to check your kidneys before and during your treatment with GLYXAMBI
- have liver problems
- have a history of inflammation of your pancreas (pancreatitis)
- have a history of infection of the vagina or penis
- have a history of urinary tract infections or problems with urination
- have any other medical condition
- are pregnant or plan to become pregnant. It is unknown if GLYXAMBI will harm your unborn baby. Tell your doctor right away if you become pregnant during treatment with GLYXAMBI
- are breastfeeding, or planning to breastfeed. It is unknown if GLYXAMBI 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. GLYXAMBI may affect the way other medicines work, and other medicines may affect how GLYXAMBI works.

Especially tell your doctor if you take:

- insulin or other medicines that can lower your blood sugar
- diuretics (water pills)
- rifampin (Rifadin[®], Rimactane[®], Rifater[®], Rifamate[®])*, an antibiotic that is used to treat tuberculosis

*These trademarks are owned by third parties not affiliated with GLYXAMBI.

What are the possible side effects of GLYXAMBI?

GLYXAMBI may cause serious side effects, including:

- **Low blood sugar (hypoglycemia)**, if you take GLYXAMBI 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 or insulin may need to be lowered. Signs and symptoms of low blood sugar may include headache, drowsiness, weakness, confusion, irritability, hunger, fast heartbeat, sweating, or feeling jittery.
- **Urinary tract infections** are a common side effect of GLYXAMBI but can sometimes be serious. Symptoms may include burning feeling when passing urine, urine that looks cloudy, and/or pain in the pelvis or back.

- **Allergic (hypersensitivity) reactions** can happen after your first dose or up to 3 months after starting GLYXAMBI. Symptoms may include swelling of your face, lips, throat, and other areas on your skin; difficulty with swallowing or breathing; raised, red areas on your skin (hives); and/or skin rash, itching, flaking, or peeling. If you have any of these symptoms, stop taking GLYXAMBI and call your doctor or go to the emergency room right away.
- **Kidney problems**, especially in people 75 years and older and people who already have kidney problems
- **Increased fats in your blood (cholesterol).**

The most common side effects of GLYXAMBI include urinary tract infections, stuffy or runny nose and sore throat, and upper respiratory tract infections.

These are not all the possible side effects of GLYXAMBI. 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.

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Visit GLYXAMBI.com for full [Prescribing Information, including Medication Guide](#).

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 146 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 2014, Boehringer Ingelheim achieved net sales of about \$16.96 billion dollars (13.3 billion euros). R&D expenditure corresponds to 19.9 percent of its net sales.

For more information please visit 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.

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 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, JARDIANCE and GLYXAMBI as treatments for patients with type 2 diabetes along with diet and exercise 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, GLYXAMBI and JARDIANCE 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® is a registered trademark of Boehringer Ingelheim

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SOURCE Eli Lilly and Company; Boehringer Ingelheim

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