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

SYNJARDY or SYNJARDY XR can cause serious side effects, including:

- **Lactic Acidosis.** Metformin hydrochloride (HCl), one of the medicines in SYNJARDY and SYNJARDY XR, 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 or SYNJARDY XR and call your healthcare provider right away or go to the nearest hospital emergency room if you get any of the following symptoms of lactic acidosis:

- feel very weak and tired
- have unusual (not normal) muscle pain
- have trouble breathing
- have unexplained stomach or intestinal problems with nausea and vomiting, or diarrhea
- have unusual sleepiness or sleep longer than usual
- feel cold, especially in your arms and legs
- feel dizzy or lightheaded
- have a slow or irregular heartbeat
- have stomach-area (abdominal) pain

You have a higher chance of getting lactic acidosis with SYNJARDY or SYNJARDY XR if you:

- have moderate to severe kidney problems.
- have liver problems.
- drink a lot of alcohol (very often or short-term “binge” drinking).
- get dehydrated (lose a large amount of body fluids). This can happen if you are sick with a fever, vomiting, or diarrhea. Dehydration can also happen when you sweat a lot with activity or exercise and do not drink enough fluids.
- have certain x-ray tests with injectable dyes or contrast agents.
- have surgery or other procedure for which you need to restrict the amount of food and liquid you eat and drink.
- have congestive heart failure.
- have a heart attack, severe infection, or stroke.
- are 65 years of age or older.

Tell your healthcare provider if you have any of the problems in the list above. Tell your healthcare provider that you are taking SYNJARDY or SYNJARDY XR before you have surgery or x-ray tests. Your healthcare provider may need to stop your SYNJARDY or SYNJARDY XR for a while if you have surgery or certain x-ray tests. SYNJARDY or SYNJARDY XR can have other serious side effects. See “What are the possible side effects of SYNJARDY or SYNJARDY XR?”

- **Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis has happened in people who have type 1 diabetes or type 2 diabetes, during treatment with empagliflozin, one of the medicines in SYNJARDY and SYNJARDY XR. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with SYNJARDY or SYNJARDY XR. Ketoacidosis is a serious condition, which needs to be treated in a hospital. Ketoacidosis may lead to death. **Ketoacidosis can happen with SYNJARDY or SYNJARDY XR even if your blood sugar is less than 250 mg/dL.** Stop taking SYNJARDY or SYNJARDY XR and call your healthcare provider right away or go to the nearest hospital emergency room if you get any of the following symptoms:

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

If you get any of these symptoms during treatment with SYNJARDY or SYNJARDY XR, if possible, check for ketones in your urine, even if your blood sugar is less than 250 mg/dL.

- **Dehydration.** SYNJARDY or SYNJARDY XR can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up (orthostatic hypotension). There have been reports of sudden worsening of kidney function in people who are taking SYNJARDY or SYNJARDY XR.

You may be at higher risk of dehydration if you:

- have kidney problems
- are 65 years of age or older
- are on low sodium (salt) diet
- take medicines to lower your blood pressure, including diuretics (water pills)

Talk to your healthcare provider about what you can do to prevent dehydration including how much fluid you should drink on a daily basis.

Talk to your healthcare provider right away if you reduce the amount of food or liquid you drink, for example if you are sick or cannot eat, or start to lose liquids from your body, for example from vomiting, diarrhea or being in the sun too...
What is SYNJARDY or SYNJARDY XR?
SYNJARDY or SYNJARDY XR is a prescription medicine that contains 2 diabetes medicines, empagliflozin (JARDIANCE) and metformin HCl.

SYNJARDY can be used along with diet and exercise to improve blood sugar in adults and children who are 10 years of age and older with type 2 diabetes.

SYNJARDY XR can be used along with diet and exercise to improve blood sugar in adults with type 2 diabetes.

One of the medicines in SYNJARDY and SYNJARDY XR, empagliflozin (JARDIANCE), can also be used in adults with type 2 diabetes:
- who have known cardiovascular disease to reduce the risk of cardiovascular death.
- who have heart failure (when the heart cannot pump enough blood to the rest of your body) to reduce the risk of cardiovascular death and hospitalization for heart failure.

SYNJARDY or SYNJARDY XR is not for people with type 1 diabetes. It may increase their risk of diabetic ketoacidosis (increased ketones in the blood or urine).

SYNJARDY or SYNJARDY XR is not for people with heart failure who do not have type 2 diabetes, because it contains the prescription medicine metformin HCl.

It is not known if SYNJARDY is safe and effective in children under 10 years of age.

It is not known if SYNJARDY XR is safe and effective in children.

Who should not take SYNJARDY or SYNJARDY XR?
Do not take SYNJARDY or SYNJARDY XR if you:
- have severe kidney problems, end stage renal disease 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 HCl, or any of the ingredients in SYNJARDY or SYNJARDY XR.

See the end of this Medication Guide for a complete list of ingredients in SYNJARDY and SYNJARDY XR. Symptoms of a serious allergic reaction to SYNJARDY and SYNJARDY XR may include:
- swelling of your face, lips, throat and other areas of your skin
- difficulty with swallowing or breathing
- raised, red areas on your skin (hives)

If you have any of these symptoms, stop taking SYNJARDY or SYNJARDY XR and call your healthcare provider right away or go to the nearest hospital emergency room.

What should I tell my healthcare provider before taking SYNJARDY or SYNJARDY XR?
Before taking SYNJARDY or SYNJARDY XR, tell your healthcare provider about all of your medical conditions, including if you:
- have kidney problems.
- have liver problems.
- have heart problems, including congestive heart failure.
- are 65 years of age or older.
- have a history of infection of the vagina or penis.
- have a history of urinary tract infection or problems with urination.
- are going to have surgery. Your healthcare provider may stop your SYNJARDY or SYNJARDY XR before you have surgery. Talk to your healthcare provider if you are having surgery about when to stop taking SYNJARDY or SYNJARDY XR and when to start it again.
- are eating less, or there is 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 or SYNJARDY XR may need to be stopped for a short time. Talk to your healthcare provider about when you should stop SYNJARDY or SYNJARDY XR and when you should start SYNJARDY or SYNJARDY XR again. See “What is the most important information I should know about SYNJARDY or SYNJARDY XR?”
- have type 1 diabetes. SYNJARDY or SYNJARDY XR should not be used to treat people with type 1 diabetes.
- have low levels of vitamin B₁₂ in your blood.
- are pregnant or plan to become pregnant. SYNJARDY or SYNJARDY XR may harm your unborn baby. If you become pregnant while taking SYNJARDY or SYNJARDY XR, tell your healthcare provider as soon as possible. Talk with your healthcare provider about the best way to control your blood sugar while you are pregnant.
- are breastfeeding or plan to breastfeed. SYNJARDY or SYNJARDY XR may pass into your breast milk and may harm your baby. Talk with your healthcare provider about the best way to feed your baby if you are taking SYNJARDY or SYNJARDY XR. Do not breastfeed while taking SYNJARDY or SYNJARDY XR.
- are a person who has not gone through menopause (premenopausal) who does not have periods regularly or at all. SYNJARDY or SYNJARDY XR can cause the release of an egg from an ovary in a person (ovulation). This can increase your chance of getting pregnant. Tell your healthcare provider right away if you become pregnant while taking...
Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SYNJARDY or SYNJARDY XR may affect the way other medicines work, and other medicines may affect how SYNJARDY or SYNJARDY XR works.

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

How should I take SYNJARDY or SYNJARDY XR?
- Take SYNJARDY or SYNJARDY XR exactly as your healthcare provider tells you to take it.
- If you are prescribed SYNJARDY:
  - take SYNJARDY by mouth 2 times each day with meals. Taking SYNJARDY with meals may lower your chance of having an upset stomach.
- If you are prescribed SYNJARDY XR:
  - take SYNJARDY XR by mouth 1 time each day with a meal in the morning. Taking SYNJARDY XR with a meal may lower your chance of having an upset stomach.
  - swallow SYNJARDY XR tablets whole. Do not break, cut, crush, dissolve, or chew SYNJARDY XR tablets. If you cannot swallow SYNJARDY XR tablets whole, tell your healthcare provider.
  - you may see something that looks like the SYNJARDY XR tablet in your stool (bowel movement). This is not harmful and should not affect the way SYNJARDY XR works to control your diabetes.
- Your healthcare provider may change your dose if needed.
- If you miss a dose, take it as soon as you remember. If you do not remember until it is time for your next dose, skip the missed dose and go back to your regular schedule. Do not take two doses of SYNJARDY or SYNJARDY XR at the same time. Talk with your healthcare provider if you have questions about a missed dose.
- Your healthcare provider may tell you to take SYNJARDY or SYNJARDY XR along with other diabetes medicines. Low blood sugar can happen more often when SYNJARDY is taken with certain other diabetes medicines. See “What are the possible side effects of SYNJARDY or SYNJARDY XR?”
- If you take too much SYNJARDY or SYNJARDY XR, call your healthcare provider or go to the nearest hospital emergency room right away.
- Your healthcare provider will do blood tests to check how well your kidneys are working before and during your treatment with SYNJARDY or SYNJARDY XR.
- When taking SYNJARDY or SYNJARDY XR, you may have sugar in your urine, which will show up on a urine test.

What should I avoid while taking SYNJARDY or SYNJARDY XR?
Avoid drinking alcohol very often, or drinking a lot of alcohol in a short period of time (“binge” drinking). It can increase your chances of getting serious side effects.

What are the possible side effects of SYNJARDY or SYNJARDY XR?
SYNJARDY or SYNJARDY XR may cause serious side effects, including:
- See “What is the most important information I should know about SYNJARDY or SYNJARDY XR?”
- Serious urinary tract infections. Serious urinary tract infections that may lead to hospitalization have happened in people who are taking empagliflozin, one of the medicines in SYNJARDY and SYNJARDY XR. Tell your healthcare provider if you have any signs or symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often, the need to urinate right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.
- Low blood sugar (hypoglycemia). In adults, if you take SYNJARDY or 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. In children who are 10 years of age and older, the risk for low blood sugar may be higher with SYNJARDY or SYNJARDY XR regardless of use with another medicine that can also lower blood sugar. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take SYNJARDY or SYNJARDY XR.
  - Signs and symptoms of low blood sugar may include:
    - headache
    - drowsiness
    - weakness
    - irritability
    - hunger
    - fast heartbeat
    - confusion
    - shaking or feeling jittery
    - dizziness
    - sweating
- A rare but serious bacterial infection that causes damage to the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum). Necrotizing fasciitis of the perineum has happened in women and men who take empagliflozin, one of the medicines in SYNJARDY and SYNJARDY XR. Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and may lead to death. Seek medical attention immediately if you have a fever or you are feeling very weak, tired or uncomfortable (malaise), and you develop any of the following symptoms in the area between and around your anus and genitals:
  - pain or tenderness
  - swelling
  - redness of skin (erythema)
- Vaginal yeast infection. Symptoms of a vaginal yeast infection include vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), or vaginal itching.
Yeast infection of the penis (balanitis or balanoposthitis). Swelling of an uncircumcised penis may develop that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include redness, itching, or swelling of the penis, rash of the penis, foul smelling discharge from the penis, or pain in the skin around the penis.

Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

Allergic (hypersensitivity) reactions. Serious allergic reactions have happened in people who are taking empagliflozin, one of the medicines in SYNJARDY and SYNJARDY XR. Symptoms may include:
- swelling of your face, lips, throat and other areas of your skin
- difficulty with swallowing or breathing
- raised, red areas on your skin (hives)

If you have any of these symptoms, stop taking SYNJARDY or SYNJARDY XR and call your healthcare provider right away or go to the nearest hospital emergency room.

Low vitamin B$_{12}$ (vitamin B$_{12}$ deficiency). Using metformin for long periods of time may cause a decrease in the amount of vitamin B$_{12}$ in your blood, especially if you have had low vitamin B$_{12}$ blood levels before. Your healthcare provider may do blood tests to check your vitamin B$_{12}$ levels.

The most common side effects of SYNJARDY or SYNJARDY XR include:
- low blood sugar
- urinary tract infection
- stuffy or runny nose and sore throat
- yeast infections in females
- diarrhea
- nausea or vomiting
- gas
- stomach discomfort
- indigestion
- weakness
- headache

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

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store SYNJARDY or SYNJARDY XR?
- Store SYNJARDY or SYNJARDY XR at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep SYNJARDY or SYNJARDY XR and all medicines out of the reach of children.

General information about the safe and effective use of SYNJARDY or SYNJARDY XR.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SYNJARDY or SYNJARDY XR for a condition for which it was not prescribed. Do not give SYNJARDY or SYNJARDY XR to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about SYNJARDY or SYNJARDY XR that is written for health professionals.

What are the ingredients in SYNJARDY?

Active Ingredients: empagliflozin and metformin HCl

Inactive Ingredients: colloidal silicon dioxide, copovidone, corn starch, and magnesium stearate. In addition, the film coating contains the following inactive ingredients: hypromellose, polyethylene glycol 400, talc, and titanium dioxide. 5 mg/500 mg and 5 mg/1,000 mg tablets also contain ferric oxide yellow. 12.5 mg/500 mg and 12.5 mg/1,000 mg tablets also contain black ferrosoferric oxide and ferric oxide red.

What are the ingredients in SYNJARDY XR?

Active Ingredients: empagliflozin and metformin HCl

Inactive Ingredients: Tablet core contains: hypromellose, magnesium stearate, and polyethylene oxide. The Film Coatings and Printing Ink contain: carnauba wax, FD&C blue#2/indigo carmine aluminum lake (12.5 mg/1,000 mg, 25 mg/1,000 mg), ferric oxide red (10 mg/1,000 mg), ferric oxide yellow (5 mg/1,000 mg, 10 mg/1,000 mg, 25 mg/1,000 mg), ferrosoferric oxide, hypromellose, isopropyl alcohol, polydextrose, polyethylene glycol, propylene glycol, purified water, talc, and titanium dioxide.

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