

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) – 1986**

This medicine is marketed upon physician's prescription only

JANUET® XR 50 mg/500 mg

Extended-release Tablets

Each extended-release tablet contains:

Sitagliptin (as phosphate salt) 50 mg

Metformin hydrochloride (extended release) 500 mg

JANUET® XR 50 mg/1000 mg

Extended-release Tablets

Each extended-release tablet contains:

Sitagliptin (as phosphate salt) 50 mg

Metformin Hydrochloride (extended release) 1000 mg

JANUET® XR 100 mg/1000 mg

Extended-release Tablets

Each extended-release tablet contains:

Sitagliptin (as phosphate salt) 100 mg

Metformin Hydrochloride (extended release) 1000 mg

For a list of inactive ingredients please refer to section 6 "Further information". See also section 2.7 "Important information about some of the ingredients of the medicine".

Read the entire leaflet carefully before using this medicine.

- This leaflet contains concise information about **JANUET XR**. If you have any further questions, refer to the doctor or pharmacist
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar
- This medicine is not intended for administration to children under 18 years of age

1. WHAT JANUET XR IS INTENDED FOR?

1.1 What is JANUET XR?

Therapeutic group: Sitagliptin: DPP-4 enzyme inhibitor. Metformin: biguanide.

1.2 What is JANUET XR used for?

JANUET XR is a tablet that contains two prescription diabetes medicines, sitagliptin (JANUVIA®) and extended-release metformin hydrochloride, which lower blood sugar levels. Sitagliptin, a member of a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors), and metformin, a member of the biguanide class of medicines, work together to control blood sugar levels in patients with type 2 diabetes mellitus, in whom this combination is appropriate.

JANUET XR is designated to lower blood sugar levels in patients with type 2 diabetes, along with diet and exercise.

2. BEFORE USING JANUET XR

2.1 Do not use JANUET XR if:

- you have type 1 diabetes mellitus
- you have severe impaired renal function (your doctor will determine the level of impairment in your renal function)
- you have diabetic ketoacidosis (increased ketones in your blood or urine: diabetes complication which includes high blood sugar, rapid weight loss, nausea or vomiting)
- you are allergic to any of the ingredients in **JANUET XR** (see section 6 "Further information" for a complete list of ingredients in **JANUET XR**)
Symptoms of a serious allergic reaction to **JANUET XR** may include: rash, raised red patches on your skin (hives), or swelling of the face, lips, tongue and throat that may cause difficulty in breathing or swallowing

2.2 Special warnings regarding use of JANUET XR

Before starting treatment with JANUET XR, tell your doctor about all of your medical conditions, including if you:

- have or have had inflammation of your pancreas (pancreatitis). If you have had pancreatitis in the past, it is not known if you have a higher chance of getting pancreatitis while you take **JANUET XR**. (see section 4 "Side effects")
- have kidney problems
- have liver problems
- have heart failure
- drink alcohol very often, or drink a lot of alcohol in short-term "binge" drinking. If you are or were addicted to alcohol
- are going to get an injection of dye or contrast agents for an x-ray procedure. **JANUET XR** may need to be stopped for a short time. Talk to your doctor about when you should stop **JANUET XR** and when you should start **JANUET XR** again. (See section 3 "How should you use **JANUET XR**?")
- have low levels of vitamin B₁₂ in your blood
- have or have had stones in your gallbladder
- have high blood triglyceride levels
- are pregnant or plan to become pregnant (see section 2.6 "Pregnancy, breastfeeding and fertility")
- are breastfeeding or plan to breastfeed (see section 2.6 "Pregnancy, breastfeeding and fertility")
- are a woman who has not gone through menopause (premenopausal) who does not have periods regularly or at all (see section 2.6 "Pregnancy, breastfeeding and fertility")

Stop taking **JANUET XR** 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 through to your back. The pain may happen with or without vomiting. These may be symptoms of pancreatitis.

2.3 Tests and follow-up

Check your blood sugar as your doctor tells you to.

Your doctor will check your diabetes with regular blood tests, including your blood sugar levels and your hemoglobin A1C.

Your doctor may do blood tests to check your vitamin B₁₂ levels.

2.4 Interactions with other medicines

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:

- Topiramate (for the treatment of convulsions and migranes)
- Acetazolamide (for the treatment of edema, glaucoma and relief of mountain sickness)
- Dolutegravir (for the treatment of HIV infection)
- Cimetidine (for the treatment of ulcers)
- Ranolazine
- Vandetanib

JANUET XR may affect the way other medicines work and other medicines may affect how **JANUET XR** works.

Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

2.5 Using JANUET XR with food

Take **JANUET XR** with meals to lower your chance of having an upset stomach. It is better to take **JANUET XR** with your evening meal.

2.6 Pregnancy, breastfeeding and fertility

- If you are pregnant or plan to become pregnant: It is not known if **JANUET XR** 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
- If you are breastfeeding or plan to breastfeed: It is not known if **JANUET XR** will pass into your breast milk. Talk with your doctor about the best way to feed your baby if you are taking **JANUET XR**
- If you are a woman who has not gone through menopause (premenopausal) who does not have periods regularly or at all: **JANUET XR** can cause the release of an egg from an ovary in a woman (ovulation). This can increase your chance of getting pregnant. Tell your doctor right away if you become pregnant while taking **JANUET XR**.

2.7 Important information about some of the ingredients of the medicine

JANUET XR contains sodium. This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE JANUET XR?

Always use **JANUET XR** according to the doctor's instructions. You should check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.

The dosage and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.

Your doctor may change your dose of **JANUET XR** if needed.

Your doctor may tell you to take **JANUET XR** along with certain other diabetes medicines. Low blood sugar (hypoglycemia) can happen more often when **JANUET XR** is taken with certain other diabetes medicines (see section 4 "Side effects").

- This medicine is not intended for administration to children under 18 years of age. Safety and effectiveness of **JANUET XR** in children under 18 years have not been established
- Take **JANUET XR** once daily with a meal to help to lower your chance of having an upset stomach. It is better to take **JANUET XR** with your evening meal
- Take **JANUET XR** tablets whole. In order to maintain the extended release properties of Januet XR, do not break, cut, crush, or chew tablets before swallowing. If you cannot swallow **JANUET XR** tablets whole, tell your doctor
- You may see something that looks like the **JANUET XR** tablet in your stool (bowel movement). If you see tablets in your stool several times, tell your doctor. Do not stop taking **JANUET XR** without talking to your doctor.

If you take more JANUET XR than you should

If you take too much **JANUET XR**, call your doctor right away.

If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you.

If you forget to take JANUET XR

If you miss a dose, take it with food 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 2 doses of **JANUET XR** at the same time.

You may need to stop taking **JANUET XR** for a short time. Call your doctor for instructions if you:

- are dehydrated (have lost too much body fluid). Dehydration can occur if you are sick with severe vomiting, diarrhea or fever, or if you drink a lot less fluid than normal
- plan to have surgery
- are going to get an injection of dye or contrast agent for an x-ray procedure (see section 2.2 "Special warnings regarding use of **JANUET XR**" and section 4 "Side effects")

When your body is under some types of stress, such as fever, trauma (such as a car accident), infection or surgery, the amount of diabetes medicine that you need may change. Tell your doctor right away if you have any of these problems and follow your doctor's instructions.

Stay on your prescribed diet and exercise program while taking **JANUET XR**.

Talk to your doctor about how to prevent, recognize and manage low blood sugar (hypoglycemia), high blood sugar (hyperglycemia), and problems you have because of your diabetes.

If you have reduced kidney function, your doctor may prescribe a lower dose.

Continue to take **JANUET XR** as long as your doctor tells you.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not discontinue use of this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take your medicine.

Wear glasses if you need them.

If you have any further questions regarding the use of this product, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, **JANUET XR** may cause side effects in some users. Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

JANUET XR may cause serious side effects, including:

4.1. Lactic Acidosis. Metformin, one of the medicines in **JANUET XR**, can cause a rare (may affect up to 1 in 10,000 people), but serious condition called lactic acidosis (a buildup of lactic acid in the blood) that can cause death. Lactic acidosis is a medical emergency and must be treated in the hospital.

Stop taking JANUET XR and call your doctor right away if you have any of the following symptoms, which could be signs of lactic acidosis:

- you feel cold in your hands or feet
- you feel dizzy or lightheaded
- you have a slow or irregular heartbeat
- you feel very weak or tired
- you have unusual (not normal) muscle pain
- you have trouble breathing
- you feel sleepy or drowsy
- you have stomach pains, nausea or vomiting

Most people who have had lactic acidosis with metformin have other things that, combined with the metformin, led to the lactic acidosis. Tell your doctor if you have any of the following, because you have a higher chance of getting lactic acidosis with **JANUET XR** if you:

- have 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 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 surgery
- have a heart attack, severe infection or stroke
- are 65 years of age or older

The best way to keep from having a problem with lactic acidosis from metformin is to tell your doctor if you have any of the problems in the list above. Your doctor may decide to stop your **JANUET XR** for a while if you have any of these things.

4.2 Pancreatitis (inflammation of the pancreas) which may be severe and lead to death.

Certain medical problems make you more likely to get pancreatitis. **Stop taking JANUET XR 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 through to your back. The pain may happen with or without vomiting. These may be symptoms of pancreatitis.

4.3 Heart failure. Heart failure means that your heart does not pump blood well enough.

Before you start taking JANUET XR, tell your doctor if you have ever had heart failure or have problems with your kidneys. **Contact your doctor right away if you have any of the following symptoms:**

- increasing shortness of breath or trouble breathing, especially when you lie down
- swelling or fluid retention, especially in the feet, ankles or legs
- an unusually fast increase in weight
- unusual tiredness

These may be symptoms of heart failure.

4.4 Kidney problems (frequency not known), sometimes requiring dialysis.

4.5 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.

4.6 Low blood sugar (hypoglycemia). Common (may affect up to 1 in 10 people). If you take **JANUET XR** with another medicine that can cause low blood sugar levels, such as a sulfonylurea or insulin, your risk of getting low blood sugar levels is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you use **JANUET XR**.

Signs and symptoms of low blood sugar may include: headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, feeling jittery.

4.7 Serious allergic reactions (frequency not known) can happen with **JANUET XR** or sitagliptin, one of the medicines in **JANUET XR**. Symptoms of a serious allergic reaction to **JANUET XR** may include: rash, raised red patches on your skin (hives), or swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing. **If you have any symptoms of a serious allergic reaction, stop taking JANUET XR and call your doctor right away or get emergency medical help.** Your doctor may give you a medicine for your allergic reaction and prescribe a different medicine for your diabetes.

4.8 Joint pain. (frequency not known). Some people who take medicines called DPP-4 inhibitors, one of the medicines in **JANUET XR**, may develop joint pain that can be severe. **Call your doctor if you have severe joint pain.**

4.9 Skin reaction. (frequency not known). Some people who take medicines called DPP-4 inhibitors, one of the medicines in **JANUET XR**, may develop a skin reaction called bullous pemphigoid that can require treatment in a hospital. **Tell your doctor right away if you develop blisters or the breakdown of the outer layer of your skin (erosion).** Your doctor may tell you to stop taking **JANUET XR**.

The most common side effects of **JANUET XR** include:

- Stuffy or runny nose and sore throat
- Upper respiratory infection
- Diarrhea
- Nausea and vomiting
- Gas, upset stomach, indigestion
- Weakness
- Headache
- Low blood sugar (hypoglycemia), when used in combination with certain medicines, such as a sulfonylurea or insulin

Taking **JANUET XR** with meals can help lessen the common stomach side effects of metformin, that usually happen at the beginning of treatment. If you have unusual or sudden stomach problems, talk with your doctor. Stomach problems that start later during treatment may be a sign of something more serious.

JANUET XR may have other side effects, including:

- **Swelling of the hands or legs.** Swelling of the hands and legs can happen if you take **JANUET XR** in combination with Thiazolidinedione (TZD) type of diabetes medicines
- Joint pain
- Muscle aches
- Arm or leg pain
- Back pain
- Itching
- Blisters

These are not all the possible side effects of **JANUET XR**. For more information, ask your doctor. Tell your doctor if you have any side effect that bothers you or does not go away.

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects:

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the homepage of the Ministry of Health's website (www.health.gov.il) which refers to the online side effects reporting form, or by using the following link:

<https://sideeffects.health.gov.il>

5. HOW TO STORE JANUET XR?

- Avoid Poisoning! This medicine, and any other medicine, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use **JANUET XR** after the expiry date (exp. date) which is stated on pack. The expiry date refers to the last day of the indicated month.
- Do not store above 25°C. Store in a dry place and keep cap tightly closed.
- Shelf life after first opening: can be used until end of expiry date.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

6.1 What JANUET XR contains?

Active ingredients: sitagliptin and metformin hydrochloride extended release.

In addition to the active ingredients, all doses of JANUET XR Tablets contain:

hypromellose, povidone, sodium stearyl fumarate, kaolin, polyethylene glycol, colloidal silicon dioxide, and propyl gallate.

Film coating contains: hypromellose, hydroxypropyl cellulose, titanium dioxide, FD&C blue #2/Indigo Carmine Aluminum Lake and carnauba wax.

JANUET XR 50 mg/500 mg Tablets also contain: microcrystalline cellulose.

JANUET XR 50 mg/1000 mg Tablets also contain: iron oxide yellow.

6.2 What JANUET XR looks like and contents of the pack

JANUET XR tablets are available in three strengths:

JANUET XR 50 mg/500 mg tablets are light blue, bi-convex, oval, film-coated tablet, debossed "78" on one side and plain on the other.

JANUET XR 50 mg/1000 mg tablets are light green, bi-convex, oval, film-coated tablet, debossed "80" on one side and plain on the other.

JANUET XR 100 mg/1000 mg tablets are blue, bi-convex, oval, film-coated tablet, debossed "81" on one side and plain on the other.

The bottle also contains a desiccant, do not swallow.

Pack sizes:

JANUET XR 50 mg/500 mg tablets: bottles of 14, 60 tablets.

JANUET XR 50 mg/1000 mg tablets: bottles of 14, 60 tablets.

JANUET XR 100 mg/1000 mg tablets: bottles of 7, 30 tablets.

Not all pack sizes may be marketed.

Manufacturer: Merck Sharp & Dohme, Corp., NJ, USA.

Marketing authorization holder: Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O. Box 7121 Petah-Tikva 49170

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Drug registration no. listed in the official registry of the Ministry of Health:

JANUET XR 50 mg/500 mg TABLETS: 151.31.33932

JANUET XR 50 mg/1000 mg TABLETS: 151.32.33933

JANUET XR 100 mg/1000 mg TABLETS: 151.33.33934