PART III: CONSUMER INFORMATION

PrJANUMET®

sitagliptin and metformin hydrochloride tablets (as sitagliptin phosphate monohydrate and metformin hydrochloride)

PrJANUMET® XR

sitagliptin and metformin hydrochloride modified-release tablets (as sitagliptin phosphate monohydrate and metformin hydrochloride)

This leaflet is Part III of a three-part "Product Monograph" published when JANUMET® and JANUMET® XR was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about JANUMET® and JANUMET® XR. Contact your physician or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
JANUMET® or JANUMET® XR are used in addition to diet and exercise to improve blood sugar levels in patients with type 2 diabetes mellitus

- Alone, in patients who are not controlled on metformin alone or currently on sitagliptin and metformin; OR
- In combination with a sulfonylurea, in patients who are not controlled on metformin and a sulfonylurea.
- JANUMET® or JANUMET® XR can be taken with premixed or long/intermediate acting insulin.
- In combination with pioglitazone, in patients who are not controlled on metformin and pioglitazone.

What it does:
JANUMET® and JANUMET® XR are a tablet that contains sitagliptin and metformin. These two medicines work together to help you achieve better blood sugar control.

Sitagliptin is a member of a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors). Sitagliptin helps to improve the levels of insulin when blood sugar level is high, especially after a meal. Sitagliptin also helps to decrease the amount of sugar made by the body. Sitagliptin is unlikely to cause low blood sugar (**hypoglycemia**).

Metformin is a member of the biguanide class of medicines, it helps to lower the amount of sugar made by the liver. Together, these medicines help you to achieve better blood sugar control.

What is type 2 diabetes?
Type 2 diabetes is a condition in which your body does not make enough insulin, and/or does not use the insulin that your body produces as well as it should. When this happens, sugar (glucose) builds up in the blood. This can lead to serious problems.

When it should not be used:
Do not take JANUMET® or JANUMET® XR if you:

- Have unstable and/or insulin-dependent (type 1) diabetes mellitus.
- Have metabolic acidosis (including diabetic ketoacidosis, history or ketoacidosis or lactic acidosis – too much acid in the blood).
- Have severe kidney disease.
- Have liver problems.
- Drink alcohol very often, or drink a lot of alcohol in the short term ("binge" drinking).
- Have severe heart problems or heart failure.
- Have a lack of oxygen in the blood. This is called hypoxemia. This can happen when you have conditions that affect your heart or breathing.
- Are stressed, have severe infections, are experiencing trauma, are about to have surgery, or are recovering from surgery.
- Have severe **dehydration** (have lost a lot of water from your body) or shock.
- Are allergic to sitagliptin, metformin, or any of the ingredients in JANUMET® or JANUMET® XR. See "What the non-medicinal ingredients are".
- Are breastfeeding.
- Are pregnant or planning to become pregnant.
- Are going to get or receive an injection of dye or contrast agent for an x-ray procedure. Talk to your physician or pharmacist about when to stop JANUMET® or JANUMET® XR and when to start again.

What the medicinal ingredients are:
Sitagliptin phosphate monohydrate and metformin hydrochloride

What the non-medicinal ingredients are:
Each film-coated tablet of JANUMET® contains the following inactive ingredients: microcrystalline cellulose, polyvinylpyrrolidone, sodium lauryl sulfate, and sodium stearyl fumarate. In addition, the film coating contains the following inactive ingredients: polyvinyl alcohol, polyethylene glycol, talc, titanium dioxide, red iron oxide, and black iron oxide.

Each modified-release tablet of JANUMET® XR contains the following inactive ingredients: colloidal silicon dioxide, hypromellose, kaolin, polyethylene glycol, povidone, propyl gallate, and sodium stearyl fumarate. The JANUMET® XR 50 mg/500 mg tablet contains the additional inactive ingredient microcrystalline cellulose. In addition, the film coating contains the following inactive ingredients: hypromellose, hydroxypropyl cellulose, titanium dioxide, FD&C Blue #2/Indigo Carmine Aluminum Lake and carnauba wax. The JANUMET® XR 50 mg/1000 mg tablet contains the additional inactive ingredient yellow iron oxide.

What dosage forms it comes in:
JANUMET® tablets contain sitagliptin/metformin hydrochloride 50 mg/500 mg, 50 mg/850 mg, or 50 mg/1000 mg.

JANUMET® XR tablets contain immediate release sitagliptin (as sitagliptin phosphate monohydrate)/extended-release metformin hydrochloride 50 mg/500 mg, 50 mg/1000 mg or 100 mg/1000 mg.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Lactic acidosis is a rare but serious buildup of acid in the blood. It can cause death. It must be treated in the hospital. JANUMET® or JANUMET® XR contains a drug called metformin hydrochloride. If you build up too much metformin in your blood you are at risk for lactic acidosis.

Alcohol increases the risk of lactic acidosis caused by metformin. Do not "binge" drink or drink alcohol often when you are taking JANUMET® or JANUMET® XR.

Lactic Acidosis

Stop taking JANUMET® or JANUMET® XR if you get the following symptoms of lactic acidosis:

- You feel very weak and tired.
- You have unusual (not normal) muscle pain.
- You have trouble breathing.
- You have stomach pain with nausea and vomiting, or diarrhea.
- You feel cold, especially in your arms and legs.
- You feel dizzy or lightheaded.
- You have a slow or irregular heartbeat.
- Your medical condition suddenly changes.

You have a higher chance of getting lactic acidosis if you:

- have severe kidney problems. Your kidneys can be affected by certain x-ray tests that use injected dye. JANUMET® or JANUMET® XR is usually stopped before and for two days after such a test. Your doctor should discuss this with you;
- have liver problems
- have congestive heart failure that requires treatment with medicines;
- drink a lot of alcohol (very often or short-term "binge" drinking);
- get **dehydration** (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 don't drink enough fluids;
- have certain x-ray tests with injectable dyes or contrast agents used;
- have surgery. Talk with your doctor before any surgery if you must restrict what you eat and drink. In these cases, JANUMET® or JANUMET® XR should be stopped for 2 days before the surgery. Wait until you are eating and drinking again before you restart JANUMET® or JANUMET® XR. You doctor should discuss this with you;
- have a heart attack, severe infection, or stroke;
- take other medications;

BEFORE or while taking JANUMET® or JANUMET® XR talk to your physician or pharmacist if:

- you are older than 65 years of age;
- you have or have had pancreatitis (inflammation of the pancreas);
- you have risk factors for pancreatitis such as:
  - gallstones (solid particles that form in the gall bladder),
  - a history of alcoholism,
  - high triglyceride levels;
- you are receiving treatment with insulin or are taking a sulfonylurea. When JANUMET® or JANUMET® XR is used in combination with sulfonylurea or insulin, low blood sugar can occur. Your physician may consider lowering the dose of the sulfonylurea or insulin. Take precautions to avoid low blood sugar while driving or using machinery;
- you have heart problems including congestive heart failure (a condition where your heart becomes weaker and less able to pump the blood that your body needs);
- you have or have had severe kidney problems;
- you have liver problems;
- you had an organ transplant;
- you have human immunodeficiency syndrome (HIV);
- you have vitamin B_{12} deficiency or anemia;
- you have hypothyroidism (low levels of thyroid hormones).

JANUMET® and JANUMET® XR are not recommended for use in patients under 18 years of age.

JANUMET® and JANUMET® XR may cause abnormal kidney function.

Cases of inflammation of the pancreas (**pancreatitis**) have been reported in patients taking JANUMET® or JANUMET® XR. Pancreatitis can be severe and lead to death.

Cases of **serious skin reactions** can occur and have been reported in patients taking JANUMET® or JANUMET® XR. These skin reactions are called **Stevens-Johnson syndrome** and **bullous pemphigoid**. They can happen after the first dose or up to 3 months on the drug. You may need treatment in a hospital. You may need to see a dermatologist to diagnose and treat these skin reactions.

INTERACTIONS WITH THIS MEDICATION

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.

If you start any new medicine, tell your healthcare professional.

The following may interact with JANUMET® or JANUMET® XR:

- Other diabetes drugs such as glyburide.
- Furosemide.
- Nifedipine (used to treat high blood pressure and chest pain).
- Drugs that decrease the rate of elimination of metformin from your body (e.g., ranolazine, vandetanib, dolutegravir and cimetidine).
- Certain "blood thinners" (phenprocoumon or other antivitamin K anticoagulants).
- Other drugs that tend to produce high blood sugar (hyperglycemia) and may lead to a loss of blood sugar control. Some example of drugs that can increase the blood sugar include:
  - Thiazide and other diuretics (water pills)
  - Corticosteroids (used to treat joint pain and swelling)
  - Phenothiazines (used to treat schizophrenia)
  - Thyroid products
  - Estrogens or estrogens plus progestogen
  - Oral contraceptives (birth control pills)
  - Phenytoin (used to treat epilepsy)
  - Nicotinic Acid
  - Sympathomimetics (used for heart problems)
  - Calcium channel blocking drugs (used for high blood pressure)
  - Isoniazid (used to treat tuberculosis)
  - Beta-2-agonists (used to treat breathing problems)
  - Carbonic anhydrase inhibitors
- ACE inhibitors drugs may lower blood glucose and the combination with JANUMET® or JANUMET® XR should be carefully monitored.

PROPER USE OF THIS MEDICATION

Your doctor will individualize your starting dose of JANUMET® or JANUMET® XR based on your current treatment regimen. Take JANUMET® or JANUMET® XR exactly as your physician has prescribed. Your physician will tell you how many JANUMET® or JANUMET® XR tablets to take and how often you should take them.

Your physician may adjust your dose, if needed to further control your blood sugar level.

Usual adult dose:
JANUMET® should be given 2 times a day by mouth with a meal to lower your chance of an upset stomach.

JANUMET® XR should be taken once a day with food preferably in the evening to lower your chance of an upset stomach.

If you take JANUMET® XR, swallow the JANUMET® XR tablets whole. Do not chew, cut, or crush the tablets. Tell your doctor if you cannot swallow JANUMET® XR whole.
You may see something that looks like the JANUMET® XR tablet in your stool (bowel movement). If this happens, check your blood sugar. If your blood sugar control has changed, contact your doctor. Do not stop taking JANUMET® XR without talking to your doctor.

Continue to take JANUMET® or JANUMET® XR as long as your physician prescribes it so you can continue to help control your blood sugar.

You may need to stop JANUMET® or JANUMET® XR for a short time. Call your physician for instructions if you:
- have a condition that may be associated with dehydration (large loss of body fluids) such as being sick with severe vomiting, diarrhea or fever, or if you drink fluids a lot less than normal;
- plan to have surgery;
- are going to get or receive an injection of dye or contrast agent for an x-ray procedure.

Overdose:

If you think you have taken too much JANUMET® or JANUMET® XR, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
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 two doses of JANUMET® or JANUMET® XR at the same time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

These are not all the possible side effects that you may have when taking JANUMET® or JANUMET® XR. If you experience any side effects not listed here, contact your healthcare professional.

Side effects of JANUMET® or JANUMET® XR include:
- Stuffy or runny nose
- Sore throat
- Gastrointestinal symptoms: diarrhea, constipation, nausea, vomiting, abdominal bloating, upset stomach, gas and loss of appetite
- Headache
- Joint pain
- Arm or leg pain
- Back pain
- Muscle aches
- Itching
- Blisters

When JANUMET® or JANUMET® XR is used with a sulfonylurea medicine or with insulin, low blood sugar (hypoglycemia) can occur. Lower doses of the sulfonylurea medicine or insulin may be required while you used JANUMET® or JANUMET® XR.

JANUMET® or JANUMET® XR can cause abnormal blood test results. Your doctor will do blood tests before you start JANUMET® or JANUMET® XR and while you take it. They may check your blood sugar, liver and thyroid function, amount of vitamin B_{12} and how well your kidneys are working. Your doctor will decide when to perform blood tests and will interpret the results.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptoms / Effects	Talk with your physician or pharmacist		Stop taking drug and call your physician or pharmacist
	Only if severe	In all cases	
Very common			
Hypoglycemia (low blood sugar - when used with a sulfonylurea or with insulin): shaking, sweating, rapid heartbeat, change in vision, hunger, headache and change in mood.		✓	
Rare			
Pancreatitis (inflammation of the pancreas): prolonged severe stomach pain and possible vomiting			✓
Allergic reactions: rash, hives, and swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing.			✓
Serious skin reactions including Stevens-Johnson syndrome, bullous pemphigoid: blisters or breakdown of your skin.		✓	
Lactic acidosis (buildup of lactic acid in the blood): malaise or a feeling of general discomfort, uneasiness or pain; feeling very weak or tired; sleepiness, drowsiness or an increasing strong desire for sleep; low blood pressure, dizziness, lightheadedness; cold hands or feet; slow or irregular heartbeat, trouble breathing; unusual muscle pain; stomach pain with nausea, vomiting, or diarrhea.			✓
Encephalopathy (disease of the brain that severely alters thinking): muscle weakness in one area, poor decision-making or concentration, involuntary twitching, trembling, difficulty speaking or swallowing, seizures.			✓
Lowering of Thyroid Stimulating hormone level in patients with low thyroid function: fatigue, feeling cold, dry skin, poor memory and concentration, weight gain.		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptoms / Effects	Talk with your physician or pharmacist		Stop taking drug and call your physician or pharmacist
	Only if severe	In all cases	
Acute kidney failure (sometimes requiring dialysis): nausea, loss of appetite and weakness, pass little or no urine, breathlessness.			✓
Hemolytic anemia (when red blood cells are destroyed faster than bone marrow can replace them): fatigue, pale color, rapid heartbeat, shortness of breath, dark urine, chills, and backache.			✓
Peripheral neuropathy (a result of damage to your peripheral nerves): gradual onset of numbness, prickling or tingling in your feet or hands, which can spread upward into your legs and arms, sharp, jabbing, throbbing, freezing or burning pain, extreme sensitivity to touch, lack of coordination and falling, muscle weakness or paralysis if motor nerves are affected.			✓
Very rare			
Vitamin B_{12} deficiency (decreased vitamin B_{12} levels in the blood): fatigue, shortness of breath, tingling or numbness of the fingers or toes, difficulty walking properly, irritability, confusion, tender calves.		✓	
Hepatitis (inflammation of the liver) or liver disorder: yellow of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

HOW TO STORE IT

The product should be stored at 15°C to 30°C.

Keep out of reach and sight of children.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by.

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about JANUMET®/JANUMET® XR:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website or Merck Canada website www.merck.ca or by calling Merck Canada at 1-800-567-2594.

To report an adverse event related to JANUMET®/ JANUMET® XR, please contact 1-800-567-2594.

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