



Before prescribing JANUMET, please read the Prescribing Information, including the Boxed Warning about lactic acidosis.



Dosage forms and strengths



JANUMET 50 mg/500 mg
50 mg sitagliptin
500 mg metformin HCl

Tablet may not print at actual size or color.



JANUMET 50 mg/1000 mg
50 mg sitagliptin
1000 mg metformin HCl

Tablet may not print at actual size or color.

Convenient Dosing Regimen to Help More Patients Meet Treatment Goals

Indications and usage

JANUMET is a dipeptidyl peptidase-4 (DPP-4) inhibitor and biguanide combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both sitagliptin and metformin is appropriate.

Important limitations of use:

- JANUMET should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- JANUMET has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis while taking JANUMET.

Dosage and administration

- The dosage of JANUMET should be individualized on the basis of the patient's current regimen, effectiveness, and tolerability while not exceeding the maximum recommended daily dose of 100 mg sitagliptin and 2000 mg metformin. Initial combination therapy or maintenance of combination therapy should be individualized and left to discretion of the health care provider. JANUMET should generally be given twice daily with meals, with gradual dose escalation, to reduce the gastrointestinal side effects due to metformin.

- » *For patients not currently being treated with metformin*, the recommended starting dose of JANUMET is 50 mg sitagliptin/500 mg metformin twice daily with gradual dose escalation to reduce the gastrointestinal side effects due to metformin.
- » *For patients currently being treated with metformin*, the starting dose of JANUMET should be sitagliptin 50 mg twice daily (100 mg total daily dose) and the dose of metformin already being taken. For patients taking metformin 850 mg twice daily, the recommended starting dose of JANUMET is 50 mg sitagliptin/1000 mg metformin twice daily.
- » *Coadministration of JANUMET with an insulin secretagogue (eg, sulfonylurea) or insulin* may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

Selected Important Risk Information

JANUMET is contraindicated in patients with renal disease or renal dysfunction (serum creatinine levels ≥ 1.5 mg/dL in males and ≥ 1.4 mg/dL in females) or abnormal creatinine clearance; acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma; or history of a serious hypersensitivity reaction to JANUMET or sitagliptin (one of the components of JANUMET), such as anaphylaxis or angioedema.

Temporarily discontinue JANUMET in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials.

Selected Important Risk Information (*cont*)

Measure renal function before initiation of therapy with JANUMET® (sitagliptin/metformin HCl) tablets and periodically thereafter. Avoid use in patients with hepatic disease. Temporarily discontinue for intercurrent serious conditions, infection, or surgery.

WARNING: LACTIC ACIDOSIS

Lactic acidosis is a rare but serious complication that can occur because of metformin accumulation. The risk increases with conditions such as sepsis, dehydration, excess alcohol intake, hepatic insufficiency, renal impairment, and acute congestive heart failure.

The onset is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, increasing somnolence, and nonspecific abdominal distress.

Laboratory abnormalities include low pH, increased anion gap, and elevated blood lactate.

If acidosis is suspected, JANUMET should be discontinued and the patient hospitalized immediately [see Warnings and Precautions].

When lactic acidosis occurs, it is fatal in approximately 50% of cases. The reported incidence of lactic acidosis in patients receiving metformin is very low (approximately 0.03 cases/1000 patient-years, with approximately 0.015 fatal cases/1000 patient-years). Reported cases have occurred primarily in diabetic patients with significant renal insufficiency, including both intrinsic renal disease and renal hypoperfusion, often in the setting of multiple concomitant medical/surgical problems and multiple concomitant medications.

There have been postmarketing reports of acute pancreatitis, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis, in patients taking JANUMET. After initiating JANUMET, observe patients carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue JANUMET and initiate appropriate management. It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis while taking JANUMET.

Use With Medications Known to Cause Hypoglycemia

Sitagliptin

When sitagliptin was used in combination with a sulfonylurea or insulin, medications known to cause hypoglycemia, the incidence of hypoglycemia was increased over that of placebo used in combination with a sulfonylurea or insulin. Therefore, patients also receiving insulin or an insulin secretagogue (eg, sulfonylurea) may require a lower dose of insulin or the insulin secretagogue to reduce the risk of hypoglycemia.

Metformin hydrochloride

Hypoglycemia does not occur in patients receiving metformin alone under usual circumstances of use but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or during concomitant use with other glucose-lowering agents (such as sulfonylureas and insulin) or ethanol. Elderly, debilitated, or malnourished patients and those with adrenal or pituitary insufficiency or alcohol intoxication are particularly susceptible to hypoglycemic effects.

There have been postmarketing reports of serious hypersensitivity reactions in patients treated with sitagliptin, one of the components of JANUMET, such as anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Onset of these reactions occurred within the first 3 months after initiation of treatment with sitagliptin, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue JANUMET, assess for other potential causes for the event, and institute alternative treatment for diabetes.

In clinical studies, the most common adverse reactions reported, regardless of investigator assessment of causality, in $\geq 5\%$ of patients and more commonly than in patients treated with placebo were as follows: diarrhea, upper respiratory tract infection, and headache (for sitagliptin and metformin combination therapy); hypoglycemia and headache (for sitagliptin in combination with metformin and sulfonylurea); hypoglycemia (for sitagliptin in combination with metformin and insulin); nasopharyngitis (for sitagliptin monotherapy); and diarrhea, nausea/vomiting, flatulence, abdominal discomfort, indigestion, asthenia, and headache (for metformin therapy).

To report SUSPECTED ADVERSE REACTIONS, contact Merck at 1-877-888-4231 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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