

## Selected Oral Agents for Type 2 Diabetes

Before prescribing JANUVIA, please read the Prescribing Information and Medication Guide.

### Insufficient insulin release



### Role of **JANUVIA**:

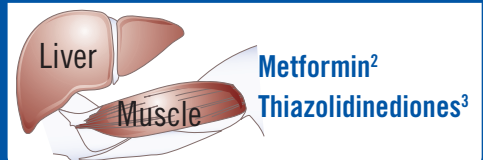
- DPP-4 rapidly degrades incretins
- JANUVIA increases and prolongs active incretin levels
- Incretins stimulate insulin release and suppress glucagon secretion in a glucose-dependent manner.

### Hepatic glucose overproduction



DPP-4=dipeptidyl peptidase-4.

### Insulin resistance



## Important Information

JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

JANUVIA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

JANUVIA 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 JANUVIA.

## Selected Important Risk Information

JANUVIA is contraindicated in patients with a history of a serious hypersensitivity reaction to sitagliptin, such as anaphylaxis or angioedema.

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

Assessment of renal function is recommended prior to initiating JANUVIA and periodically thereafter. A dosage adjustment is recommended in patients with moderate or severe renal insufficiency and in patients with end-stage renal disease requiring hemodialysis or peritoneal dialysis. Caution should be used to ensure that the correct dose of JANUVIA is prescribed.

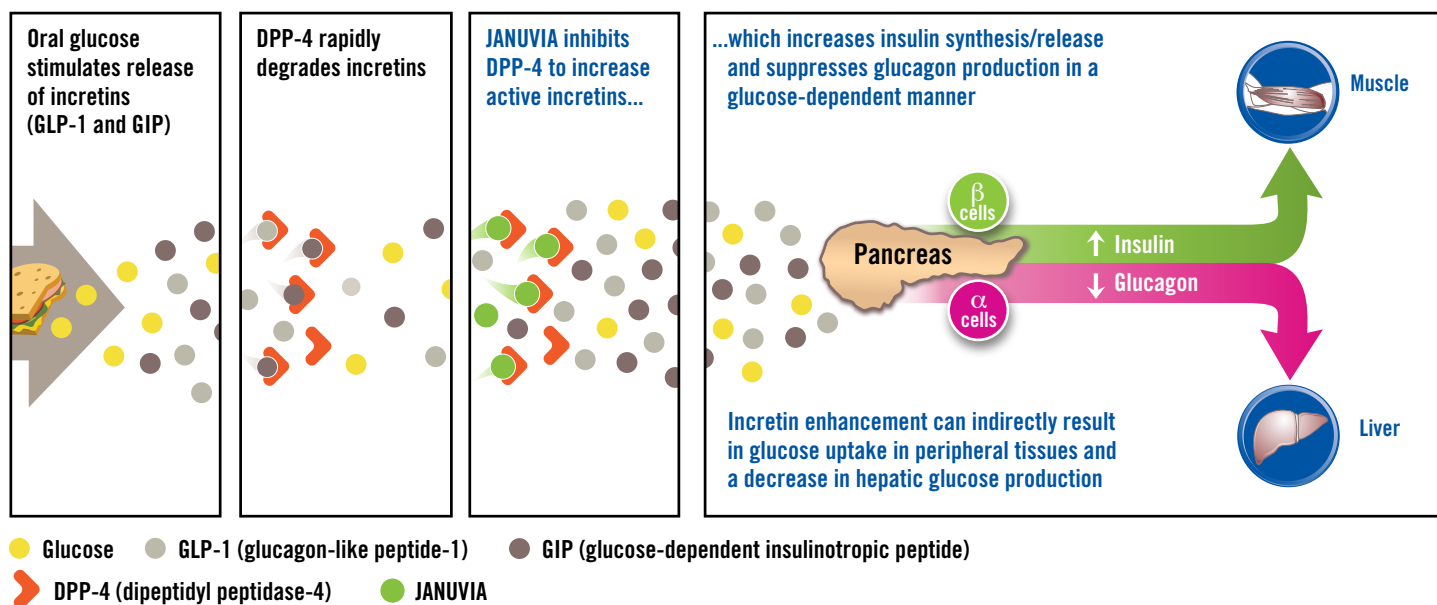
There have been postmarketing reports of worsening renal function, including acute renal failure, sometimes requiring dialysis. A subset of these reports involved patients with renal insufficiency, some of whom were prescribed inappropriate doses of sitagliptin.

When JANUVIA was used in combination with a sulfonyleurea or insulin, medications known to cause hypoglycemia, the incidence of hypoglycemia was increased over that of placebo. Therefore, a lower dose of sulfonyleurea or insulin may be required to reduce the risk of hypoglycemia.

*(Selected Important Risk Information continued on next page.)*

# JANUVIA® (sitagliptin) tablets targets 2 core defects of diabetes in a glucose-dependent manner

## Glucose-dependent mechanism targets 2 core defects: insufficient insulin release and hepatic glucose overproduction



### Selected Important Risk Information (*continued*)

The incidence (and rate) of hypoglycemia based on all reports of symptomatic hypoglycemia were: 12.2% (0.59 episodes/patient-year) for JANUVIA 100 mg in combination with glimepiride (with or without metformin), 1.8% (0.24 episodes/patient-year) for placebo in combination with glimepiride (with or without metformin), 15.5% (1.06 episodes/patient-year) for JANUVIA 100 mg in combination with insulin (with or without metformin), and 7.8% (0.51 episodes/patient-year) for placebo in combination with insulin (with or without metformin).

There have been postmarketing reports of serious hypersensitivity reactions in patients treated with JANUVIA, 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 JANUVIA, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue JANUVIA, assess for other potential causes for the event, and institute alternative treatment for diabetes.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with JANUVIA or with any other antidiabetic drug.

In clinical studies, the adverse reactions reported, regardless of investigator assessment of causality, in  $\geq 5\%$  of patients treated with JANUVIA as monotherapy and in combination therapy and more commonly than in patients treated with placebo, were upper respiratory tract infection, nasopharyngitis, and headache.

**Before prescribing JANUVIA, please read the Prescribing Information and Medication Guide, available at [Januvia.com/hcp](http://Januvia.com/hcp).**

#### References:

1. Glucotrol [package insert]. New York, NY: Pfizer Inc; 2006.
2. Glucophage [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2009.
3. Actos [package insert]. Osaka, Japan: Takeda Pharmaceutical Company Limited; 2007.

