



Dear Doctor:

Thank you for your interest in the enclosed reprint, "Effect of the Dipeptidyl Peptidase-4 Inhibitor Sitagliptin as Monotherapy on Glycemic Control in Patients With Type 2 Diabetes," by P. Aschner et al, as published in *Diabetes Care*, Volume 29, Number 12, December 2006. The objective of the study was to examine the efficacy and safety of once-daily oral sitagliptin as monotherapy in patients with type 2 diabetes.

Although the authors remark that preclinical animal studies have shown that dipeptidyl peptidase-4 (DPP-4) inhibitors stimulate beta-cell neogenesis and survival, these effects have not been demonstrated in human clinical trials.

Although this paper provides data on 200 mg of sitagliptin given once daily, the recommended dose of JANUVIA™ (sitagliptin) tablets is 100 mg once daily.

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

JANUVIA is indicated to improve glycemic control, in combination with metformin or a thiazolidinedione, in patients with type 2 diabetes when the single agent alone, with diet and exercise, does not provide adequate glycemic control.

JANUVIA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

A dosage adjustment is recommended in patients with moderate or severe renal insufficiency or with end-stage renal disease requiring hemodialysis or peritoneal dialysis.

The adverse reactions, regardless of investigator assessment of causality, in $\geq 5\%$ of patients treated with JANUVIA and more commonly than in patients treated with placebo, were upper respiratory tract infection, nasopharyngitis, and headache.

Before prescribing JANUVIA, please read the accompanying full Prescribing Information.

Thank you for your interest in this information about JANUVIA.

Sincerely,

A handwritten signature in black ink, appearing to read "Bram Greenberg".

Bram Greenberg, MD, FAAP
Executive Director, Medical Services

[Click to view Study Abstract](#)

Enclosures: 20607960(4)-JAN
Full Prescribing Information for JANUVIA

Effect of the Dipeptidyl Peptidase-4 Inhibitor Sitagliptin as Monotherapy on Glycemic Control in Patients With Type 2 Diabetes

PABLO ASCHNER, MD¹
MARK S. KIPNES, MD²
JARED K. LUNCEFORD, PHD³
MATILDE SANCHEZ, PHD³

CAROLYN MICKEL, MS³
DEBORA E. WILLIAMS-HERMAN, MD³
FOR THE SITAGLIPTIN STUDY 021 GROUP*

OBJECTIVE — To examine the efficacy and safety of once-daily oral sitagliptin as monotherapy in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS — In a randomized, double-blind, placebo-controlled study, 741 patients (baseline HbA_{1c} [A1C] 8.0%) were randomized to sitagliptin 100 or 200 mg or placebo for 24 weeks.

RESULTS — Sitagliptin 100 and 200 mg produced significant ($P < 0.001$) placebo-subtracted reductions in A1C (-0.79 and -0.94% , respectively) and fasting plasma glucose (-1.0 mmol/l [-17.1 mg/dl] and -1.2 mmol/l [-21.3 mg/dl], respectively). Patients with baseline A1C $\geq 9\%$ had greater reductions in placebo-subtracted A1C with sitagliptin 100 and 200 mg (-1.52 and -1.50% , respectively) than those with baseline A1C $< 8\%$ (-0.57 and -0.65%) or ≥ 8 to $< 9.0\%$ (-0.80 and -1.13% , respectively). In a meal tolerance test, sitagliptin 100 and 200 mg significantly decreased 2-h postprandial glucose (PPG) (placebo-subtracted PPG -2.6 mmol/l [-46.7 mg/dl] and -3.0 mmol/l [-54.1 mg/dl], respectively). Results for the above key efficacy parameters were not significantly different between sitagliptin doses. Homeostasis model assessment of β -cell function and proinsulin-to-insulin ratio improved with sitagliptin. The incidence of hypoglycemia was similar, and overall gastrointestinal adverse experiences were slightly higher with sitagliptin. No meaningful body weight changes from baseline were observed with sitagliptin 100 (-0.2 kg) or 200 mg (-0.1 kg). The body weight change with placebo (-1.1 kg) was significantly ($P < 0.01$) different from that observed with sitagliptin.

CONCLUSIONS — In this 24-week study, once-daily sitagliptin monotherapy improved glycemic control in the fasting and postprandial states, improved measures of β -cell function, and was well tolerated in patients with type 2 diabetes.

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