

Five Models Assess Readiness to Change Behaviors

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SAN DIEGO — As pay for performance becomes more common, patient adherence could become a pocketbook issue for physicians, Dr. Robert F. Kushner said at the annual meeting of the American College of Physicians.

"A patient's behavior is shaped by their environment, lifestyle, and life experiences. People do what they do for a reason. No

one is a bad patient," said Dr. Kushner, a professor of medicine at Northwestern University, Chicago. "Your role is to find out why they're doing what they're doing."

The first step is assessing the patient's readiness for change. But just asking a patient if he or she is ready isn't enough. "Very few patients want to be bad patients in front of your eyes," he said. "Very few patients will say, 'No, I'm not ready, doctor.'"

Go deeper in understanding their readiness by evaluating their reasons and mo-

tivation to change behavior, previous attempts at change, the level of support expected from family and friends, and potential barriers. In addition, assessing whether patients have the time available to make the change is critical.

There are some tools available to help physicians make that assessment, Dr. Kushner said. Five models for understanding and changing behavior have been around since the 1970s: health belief model, self-determination, motivational inter-

viewing, social cognitive theory/ecological models, and stages of change.

"Intuition is not enough," he said. "It really helps to know the theories and models and approaches that have been developed to help us understand why we do what we do."

► **Health belief model.** Under this model, the patient might not understand the importance of making a behavioral or lifestyle change, or might be ignoring health risks. It is often helpful to educate this type of patient about susceptibility to risks, Dr. Kushner said.

► **Self-determination.** This involves the goal of helping patients find their own personal motivation for making a change. In general, patients are more likely to adopt healthy behaviors because they want to, not because they should or they have to.

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Dr. Kushner said he often evaluates patient motivation by asking them to assess, on a scale of 0-10, how hard it is to make the change. Patients who respond that the difficulty is about a 10 are unlikely to be able to main-

tain the change, he said.

► **Motivational interviewing.** With motivational interviewing, physicians can assess a patient's readiness to change by asking two questions: How important is this change on a scale of 0-10? How confident are you that you can make the change on a scale of 0-10? Typically, the confidence number will be lower than the importance number. That opens up a dialogue for the physician to ask what can be done to improve confidence.

The goal with motivational interviewing is to support the patients' own belief that change is possible, Dr. Kushner said, but not to get angry or argue with the patient.

► **Social cognitive theory/ecological models.** These models look at the resources for or barriers to the patient making the change. "This is the most important theory I use on a daily basis," he said. "It looks at the patient in the context of their life, their community, and their environment." For example, can the patient afford to make changes to his or her diet? The social cognitive theory model also depends on the patient's self-efficacy and the degree to which the patient believes that making changes will lead to a positive outcome.

► **Stages of change.** Under the stages of change model, the physician assesses the patients' readiness for change and tries to support movement to the next stage. The five stages of change are precontemplation, contemplation, preparation, action, and maintenance. The stages of change can be very helpful in choosing the most effective way to approach the patient, he said. For example, when patients are in the precontemplation stage, provide education and move on. ■

Digoxin

There was a slight increase in the area under the curve (AUC, 11%) and mean peak drug concentration (C_{max} , 18%) of digoxin with the coadministration of 100 mg sitagliptin for 10 days. These increases are not considered likely to be clinically meaningful. Digoxin, as a cationic drug, has the potential to compete with metformin for common renal tubular transport systems, thus affecting the serum concentrations of either digoxin, metformin or both. Patients receiving digoxin should be monitored appropriately. No dosage adjustment of digoxin or JANUMET is recommended.

Glyburide

In a single-dose interaction study in type 2 diabetes patients, coadministration of metformin and glyburide did not result in any changes in either metformin pharmacokinetics or pharmacodynamics. Decreases in glyburide AUC and C_{max} were observed, but were highly variable. The single-dose nature of this study and the lack of correlation between glyburide blood levels and pharmacodynamic effects make the clinical significance of this interaction uncertain.

Furosemide

A single-dose, metformin-furosemide drug interaction study in healthy subjects demonstrated that pharmacokinetic parameters of both compounds were affected by coadministration. Furosemide increased the metformin plasma and blood C_{max} by 22% and blood AUC by 15%, without any significant change in metformin renal clearance. When administered with metformin, the C_{max} and AUC of furosemide were 31% and 12% smaller, respectively, than when administered alone, and the terminal half-life was decreased by 32% without any significant change in furosemide renal clearance. No information is available about the interaction of metformin and furosemide when coadministered chronically.

Nifedipine

A single-dose, metformin-nifedipine drug interaction study in normal healthy volunteers demonstrated that coadministration of nifedipine increased plasma metformin C_{max} and AUC by 20% and 9%, respectively, and increased the amount excreted in the urine. T_{max} and half-life were unaffected. Nifedipine appears to enhance the absorption of metformin. Metformin had minimal effects on nifedipine.

The Use of Metformin with Other Drugs

Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. When such drugs are administered to a patient receiving JANUMET the patient should be closely observed to maintain adequate glycemic control.

In healthy volunteers, the pharmacokinetics of metformin and propranolol, and metformin and ibuprofen were not affected when coadministered in single-dose interaction studies.

Metformin is negligibly bound to plasma proteins and is, therefore, less likely to interact with highly protein-bound drugs such as salicylates, sulfonamides, chloramphenicol, and probenecid, as compared to the sulfonylureas, which are extensively bound to serum proteins.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B:

JANUMET

There are no adequate and well-controlled studies in pregnant women with JANUMET or its individual components; therefore, the safety of JANUMET in pregnant women is not known. JANUMET should be used during pregnancy only if clearly needed.

Merck & Co., Inc. maintains a registry to monitor the pregnancy outcomes of women exposed to JANUMET while pregnant. Health care providers are encouraged to report any prenatal exposure to JANUMET by calling the Pregnancy Registry at (800) 986-8999.

No animal studies have been conducted with the combined products in JANUMET to evaluate effects on reproduction. The following data are based on findings in studies performed with sitagliptin or metformin individually.

Sitagliptin

Reproduction studies have been performed in rats and rabbits. Doses of sitagliptin up to 125 mg/kg (approximately 12 times the human exposure at the maximum recommended human dose) did not impair fertility or harm the fetus. There are, however, no adequate and well-controlled studies with sitagliptin in pregnant women.

Sitagliptin administered to pregnant female rats and rabbits from gestation day 6 to 20 (organogenesis) was not teratogenic at oral doses up to 250 mg/kg (rats) and 125 mg/kg (rabbits), or approximately 30 and 20 times human exposure at the maximum recommended human dose (MRHD) of 100 mg/day based on AUC comparisons. Higher doses increased the incidence of rib malformations in offspring at 1000 mg/kg, or approximately 100 times human exposure at the MRHD.

Sitagliptin administered to female rats from gestation day 6 to lactation day 21 decreased body weight in male and female offspring at 1000 mg/kg. No functional or behavioral toxicity was observed in offspring of rats.

Placental transfer of sitagliptin administered to pregnant rats was approximately 45% at 2 hours and 80% at 24 hours postdose. Placental transfer of sitagliptin administered to pregnant rabbits was approximately 66% at 2 hours and 30% at 24 hours.

Metformin hydrochloride

Metformin was not teratogenic in rats and rabbits at doses up to 600 mg/kg/day. This represents an exposure of about 2 and 6 times the maximum recommended human daily dose of 2000 mg based on body surface area comparisons for rats and rabbits, respectively. Determination of fetal concentrations demonstrated a partial placental barrier to metformin.

Nursing Mothers

No studies in lactating animals have been conducted with the combined components of JANUMET. In studies performed with the individual components, both sitagliptin and metformin are secreted in the milk of lactating rats. It is not known whether sitagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when JANUMET is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of JANUMET in pediatric patients under 18 years have not been established.

Geriatric Use

JANUMET Because sitagliptin and metformin are substantially excreted by the kidney and because aging can be associated with reduced renal function, JANUMET should be used with caution as age increases. Care should be taken in dose selection and should be based on careful and regular monitoring of renal function [see Warnings and Precautions].

Sitagliptin

Of the total number of subjects (N=3884) in Phase II and III clinical studies of sitagliptin, 725 patients were 65 years and over, while 61 patients were 75 years and over. No overall differences in safety or effectiveness were observed between subjects 65 years and over and younger subjects. While this and other reported clinical experience have not identified differences in responses between the elderly and younger patients, greater sensitivity of some older individuals cannot be ruled out.

Metformin hydrochloride

Controlled clinical studies of metformin did not include sufficient numbers of elderly patients to determine whether they respond differently from younger patients, although other reported clinical experience has not identified differences in responses between the elderly and young patients. Metformin should only be used in patients with normal renal function. The initial and maintenance dosing of metformin should be conservative in patients with advanced age, due to the potential for decreased renal function in this population. Any dose adjustment should be based on a careful assessment of renal function [see Contraindications, Warnings and Precautions].



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