

## Kaplan USMLE Step 1: Follow-up for woman with type 2 diabetes

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If you're preparing for the United States Medical Licensing Examination<sup>®</sup> (USMLE<sup>®</sup>) Step 1 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

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### This month's stumper

A 63-year-old woman with type 2 diabetes mellitus comes to the physician for a follow-up examination. She states that she has attempted diet control and exercise for the last nine months. She has a history of heart failure, hypertension and hypercholesterolemia.

She currently takes enalapril and low-dose aspirin and has no drug allergies. Laboratory studies show a creatinine of 2.2 mg/dL and a hemoglobin A1c of 8.9%.

Which of the following is the most appropriate initial pharmacotherapy for this patient?

- A. Glimepiride.
- B. Metformin.
- C. Metformin and glipizide.
- D. Pramlintide.

E. Rosiglitazone.

The correct answer is A.

## Kaplan Medical explains why

The initial decision about the choice of drug to manage hyperglycemia must take into account the comorbidities of the patient and the relative contraindications of the drug. Insulin secretagogues such as sulfonylureas (glipizide, glyburide, glimepiride),  $\alpha$ -glucosidase inhibitors (miglitol, acarbose), thiazolidinediones ("glitazones") (pioglitazone, rosiglitazone), biguanides (metformin), and insulin all are approved for monotherapy for diabetes.

Most patients are initially started on metformin unless there is a contraindication, such as renal dysfunction (as seen in this patient). Sulfonylureas, DPP-4 inhibitors (sitagliptin), GLP-1 agonists (exenatide) or glitazones (rosiglitazone) are generally used as second line agents when metformin is

unsuccessful or cannot be used. In this patient, the most recommended initial treatment would be the sulfonylurea glimepiride.

## Why the other answers are wrong

**Choices B and C:** Metformin, a biguanide, has a rare but serious complication of lactic acidosis. Despite this risk, it is the drug of choice for type 2 diabetes. A primary reason to use another agent in place of metformin is when the patient is at risk for developing metformin-induced lactic acidosis.

The risk of lactic acidosis (secondary to metformin) is increased in patients with heart failure, liver disease, severe hypoxia, any form of acidosis, intravenous contrast agent administration, and renal insufficiency (as seen in this patient with a creatinine of 2.2 mg/dL). It is recommended that use of metformin be avoided in men with creatinine greater than 1.5 mg/dL and in women with creatinine more than 1.4 mg/dL.

**Choice D:** Pramlintide is an amylin mimetic that suppresses plasma glucagon secretion, slows gastric emptying, and promotes satiety, thereby decreasing postprandial glucose rise. Aside from insulin, it is the only medication currently approved for use in both type 1 and type 2 diabetes. Pramlintide is generally reserved for type 2 diabetes patients unresponsive to traditional therapies.

Current treatment guidelines have this medication listed as a second- or third-line therapy for type 2 diabetes. It can be used safely in patients with renal dysfunction.

**Choice E:** Thiazolidinediones such as rosiglitazone reduce insulin resistance by binding PPAR receptors, and older generations of this class of drugs are associated with liver toxicity. Thiazolidinediones are associated with exacerbations of congestive heart failure and peripheral edema. Hence, it is contraindicated for use in patients (such as this patient) with a history of heart failure.

## Tips to remember

- Glimepiride is a second-generation sulfonylurea that undergoes hepatic clearance and is safer to use in patients with renal dysfunction than metformin.
- Sulfonylureas are indicated in patients with type 2 diabetes when their diabetes cannot be controlled with metformin, diet and exercise alone.
- Metformin should not be used in patients with renal insufficiency or heart failure, conditions that predispose patients to hypoxemia or lactic acidosis.

For more prep questions on USMLE Steps 1, 2 and 3, view other posts in this series.