Diabetes is the leading cause of chronic kidney disease (CKD) in the United States as a result of its deleterious effects on the microvasculature of the renal system. Approximately 40% of people with diabetes, and 18% of people with prediabetes, also have CKD/renal impairment. Intensive therapy for both diabetes and CKD/renal impairment is critical to optimize the health of patients with both conditions. Management of type 2 diabetes mellitus (T2DM) involves a multifactorial approach that includes meal planning, physical activity, and pharmacologic treatment, each of which may need to be modified in the setting of CKD.

**GLYCEMIC GOALS FOR PATIENTS WITH CKD/RENAL IMPAIRMENT**

Hyperglycemia is the fundamental cause of microvascular complications in the kidney. While poor glycemic control is associated with the development of elevated albuminuria in T2DM, intensive treatment of hyperglycemia reduces the development of microalbuminuria, may slow the progression of established CKD/renal impairment, and reduces the rate of reduction in glomerular filtration rate.

The target glycosylated hemoglobin (A1C) for most patients with diabetes, with or without kidney disease, is <7%. The therapeutic targets of antidiabetic agents aim to reduce insulin resistance, increase insulin secretion, restrain glucagon secretion, or slow carbohydrate digestion. In the liver, metformin and the thiazolidinediones (TZDs) are potent insulin sensitizers; they also suppress glucose production. Incretin-based therapies, such as glucagon-like peptide-1 (GLP-1) receptor agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors, suppress glucose production through the incretin pathway. TZDs and metformin also act in skeletal muscle to increase glucose uptake. In adipose tissue, TZDs again act as insulin sensitizers to increase glucose uptake and reduce free fatty acid production. In the gastrointestinal tract, alpha-glucosidase inhibitors suppress the breakdown of carbohydrates, reducing glycemic load, while GLP-1 receptor agonists and possibly DPP-4 inhibitors slow gastric emptying.

In the pancreas, sulfonylureas (SUs) and non-sulfonylurea secretagogues (glinides), GLP-1 receptor agonists, and DPP-4 inhibitors stimulate insulin secretion. GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) elicit glucose-dependent actions to stimulate insulin secretion and inhibit glucagon secretion.

Other agents include exogenous insulin preparations, ie, long- and intermediate-acting basal insulins, rapid-acting insulin

**CONSIDERATIONS FOR GLUCOSE-LOWERING THERAPY IN PATIENTS WITH CKD/RENAL IMPAIRMENT**

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Other agents include exogenous insulin preparations, ie, long- and intermediate-acting basal insulins, rapid-acting insulin
analogs, and regular insulin for prandial use. Pramlintide, an analog of human amylin, is approved for use with prandial insulin to lower postprandial blood glucose, delay gastric emptying, and provide satiety. More recently, the bile acid sequestrant colesevelam and the dopamine agonist bromocriptine were approved for the treatment of T2DM.6,7

Because several classes of antidiabetic agents are metabolized and excreted by renal mechanisms, they may be contraindicated, not recommended, or require dose adjustment for patients with Stage 3, 4, or 5 kidney disease (Table).1 These include the biguanide metformin, first-generation SUs, and most DPP-4 inhibitors.1 In contrast, second-generation SUs, TZDs, and alpha-glucosidase inhibitors that undergo hepatic or gastrointestinal metabolism do not require dose adjustment in renal impairment.1,9

Renal function should be assessed before prescribing any new antidiabetic agent and monitored routinely for any changes that may affect treatment.1

### REFERENCES