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## Optimizing CKD Management: Aligning with Guidelines and SGLT2 Inhibitor's Role

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Sodium-glucose co-transporter-2 (SGLT2) inhibitors have recently emerged as an effective means to protect kidney function in people with chronic kidney disease (CKD). SGLT2 inhibitors specifically inhibit sodium and glucose reabsorption in the early proximal tubule of the renal nephron, and in doing so protect the tubule, reduce nephron dropout and slow progressive GFR decline through pathways common to all forms of kidney disease, and independent to effects on glucose control, weight or blood pressure. Although originally developed as glucose-lowering agents, it became apparent in cardiovascular outcome trials that the trajectory of kidney function decline was significantly slowed and the incidence of serious falls in kidney function was reduced in participants receiving an SGLT2 inhibitor. Reductions in heart failure, hospitalization and cardiovascular mortality were also observed with SGLT2 inhibitors, with the greatest absolute benefits seen in participants with CKD. These observations have led to specific outcome trials in participants with CKD, including DAPA-CKD, CREDENCE and most recently, EMPA-KIDNEY. Real-world studies have further confirmed the observation of kidney benefits. In response, recent global KDIGO Guidelines have recommended the use of SGLT2 inhibitors as first line therapy in patients with CKD, alongside statins, renin-angiotensin-aldosterone system inhibitors and multifactorial risk factor management as indicated. However, SGLT2 inhibitors remain significantly underutilized in the setting of CKD. Indeed, an inertia paradox exists, with patients with more severe disease less likely to receive an SGLT2 inhibitor. But safety concerns appear unfounded, as acute kidney injury, hyperkalaemia, major acute cardiovascular events and cardiac death in patients with CKD all appear to be lower following SGLT2 inhibition. In all patients with and at risk of CKD, early treatment with an SGLT2 inhibitor should be

strongly considered well before irreversible nephron losses consign patients with advanced CKD to poor clinical outcomes.

**Keywords:** SGLT2, Chronic kidney disease, diabetic kidney disease, diabetic nephropathy, diabetic complications