Individualizing drug therapy in patients with diabetes and chronic kidney disease

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5 steps for ensuring optimal drug dosing in patients with chronic kidney disease¹

1. Estimate renal function using creatinine clearance or eGFR

2. Review ALL medications a patient is taking. It is important to look for:

- Medications that are renally eliminated and/or have metabolites that are renally eliminated.
- Medications with a potential for increased risk of adverse effects (e.g., hyperkalemia with angiotensin-converting enzyme [ACE] inhibitors and angiotensin II receptor blockers [ARB] and other medications that raise potassium).
- Medications with a potential for drug interactions.
- Medications where there may be decreased therapeutic response (e.g., thiazide diuretics in CKD stages 4 and 5).
- Medications with the potential for nephrotoxicity (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]).

3. Calculate an individualized dosing regimen based on the patient's treatment goals and degree of kidney function. In some cases, alternative therapy may be required.

4. Monitor for efficacy and toxicity and adjust the new regimen as needed based on the patient's response.

5. Advise all patients about the sick day medication list.²

Dosing considerations for antihyperglycemics in chronic kidney disease³⁻⁸

	CKD 1 and 2 eGFR ≥60 mL/min	CKD 3 eGFR 30-59 mL/min	CKD 4 eGFR 15-29 mL/min	CKD 5 eGFR <15 mL/min or dialysis	Comments
Metformin	No dose adjustment	Reduce dose	Use alternative agent		Risk of drug accumulation with declining renal function, especially if acute.
Alpha-glucosidase inhibitor					
Acarbose	No dose adjustment	No dose adjustment	Use alternative agent		
DPP4-inhibitors					
Alogliptin	No dose adjustment	Lower dose 12.5 mg daily (30-49 mL/min)	Lower dose 6.25 mg daily		Can be given without regard to timing of dialysis but experience is limited.
Linagliptin	No dose adjustment required				Experience in patients with end-stage renal disease or on dialysis is limited. Use with caution in these patients.
Saxagliptin	No dose adjustment	Lower dose 2.5 mg once daily (<50 mL/min)		Use alternative agent.	Should not be used in patients on dialysis.
Sitagliptin	No dose adjustment	Lower dose 50 mg daily (30-49 mL/min)	Use lowest dose 25 mg daily		

	CKD 1 and 2 eGFR $\geq$ 60 mL/min	CKD 3 eGFR 30-59 mL/min	CKD 4 eGFR 15-29 mL/min	CKD 5 eGFR <15 mL/min or dialysis	Comments
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GLP-1 receptor agonists

Albiglutide	No dose adjustment			Caution when initiating or increasing doses in patients with renal impairment. Monitor renal function in patients with renal impairment reporting severe GI reactions which may worsen renal function.
Exenatide	No dose adjustment	Lower dose 5 mcg bid	Use alternative agent	
Liraglutide	No dose adjustment	Use alternative agent (<50 mL/min)		

Meglitinides

Nateglinide	No dose adjustment required				
Repaglinide	No dose adjustment required				

Sulfonylureas

Gliclazide	No dose adjustment		Risk of hypoglycemia, consider lower dose	Risk of hypoglycemia, consider alternative agent	Experience in patients with end-stage renal disease or on dialysis is limited. Use with caution in these patients.
Glimepiride	No dose adjustment		Risk of hypoglycemia, consider lower dose	Max 1 mg daily, consider alternative agent	Both pharmacokinetics and pharmacodynamics are altered, increasing risk of hypoglycemia.
Glyburide	No dose adjustment	Use alternative agent			Increased risk of prolonged hypoglycemia due to accumulation of parent drug and active metabolites.

Thiazolidinediones (TZDs)

Pioglitazone	No dose adjustment required	Theoretical risk of volume overload
Rosiglitazone	No dose adjustment required	

	CKD 1 and 2 eGFR ≥60 mL/min	CKD 3 eGFR 30-59 mL/min	CKD 4 eGFR 15-29 mL/min	CKD 5 eGFR <15 mL/min or dialysis	Comments
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SGLT2 inhibitors

Canagliflozin	No dose adjustment	Do not initiate. Can maintain at 100 mg daily if already taking (45-60 mL/min).	Use alternative agent	Ineffective and increased risk of adverse effects if eGFR <45 mL/min
Dapagliflozin	No dose adjustment	Use alternative agent		Ineffective and increased risk of adverse effects if eGFR <60 mL/min
Empagliflozin	No dose adjustment	Do not initiate. Can maintain if already taking (45-60mL/min).	Use alternative agent	Ineffective and increased risk of adverse effects if eGFR < 45mL/min

Adapted with permission from Appendix 6 of the *CDA Clinical Practice Guidelines*.

For more information, go to www.diabetespharmacistsnetwork.ca and check out the Banting & Best Diabetes Centre's new Interactive Learning Program. First case in the series is on CKD and diabetes!

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