Therapeutic considerations when using common therapies in patients with diabetes with varying degrees of renal impairment

Antihyperglycemic Therapies

	CKD 1 & 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		See "Sick Day Medication List" (Appendix 7). 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 to 12.5 mg daily (<50 mL/min)	Use lowest dose (6.25 mg daily)		
Linagliptin	No dose adjustment required				Experience in patients with ESRD 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)		Risk of accumulation.
GLP-1 Receptor Agonists					
Albiglutide	No dose adjustment required				Use caution when initiating or escalating doses in patients with renal impairment
Exenatide	No dose adjustment	Lower dose (5 mcg BID)	Use alternative agent		
Liraglutide	No dose adjustment	Use alternative agent (<50 mL/min)			
Insulin Secretagogues					
Gliclazide	No dose adjustment		Risk of hypoglycemia, consider lower dose	Risk of hypoglycemia, consider alternative agent	
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.
Nateglinide	No dose adjustment required				
Repaglinide	No dose adjustment required				

		CKD 1 & 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
Antihyperglycemic Therapies	**SGLT2 inhibitors**					
	Canagliflozin	No dose adjustment	Lower dose to 100 mg daily and stop if eGFR <45 mL/min	Use alternative agent		See "Sick Day Medication List" (Appendix 7). Reduced glycemic efficacy at lower renal function.
	Dapagliflozin	No dose adjustment	Use alternative agent			See "Sick Day Medication List" (Appendix 7). Reduced glycemic efficacy at lower renal function
	Empagliflozin	No dose adjustment	Close monitoring of renal function recommended. Stop if eGFR < 45 mL/min	Use alternative agent		See "Sick Day Medication List" (Appendix 7). Reduced glycemic efficacy at lower renal function
	Thiazolidinediones (TZDs)					
	Pioglitazone	No dose adjustment required				Risk of volume overload.
	Rosiglitazone	No dose adjustment required				
Lipid Lowering Therapies	**Bile Acid Sequestrant**					
	Cholestyramine	No dose adjustment required				
	Cholesterol Absorption Inhibitor					
	Ezetimibe	No dose adjustment required				
	Nicotinic Acid (niacin)	No dose adjustment	50% of total daily dose administered as divided doses		25% of total daily dose administered in divided doses	
	Fibrates	*Risk of rhabdomyolisis when fibrates used in combination with statins is increased in CKD and, therefore, combination should be avoided.*				
	Bezafibrate	No dose adjustment	Use alternative agent			
	Fenofibrate	No dose adjustment	Reduce dose		Use alternative agent	Fenofibrate micronized should not be used as initial treatment in CKD. Initiate with Lipidil EZ 48 mg/day.
	Gemfibrozil	No dose adjustment	Use alternative agent			Concomitant use of gemfibrozil and repaglinide should be avoided as can result in hypoglycemia.

		CKD 1 & 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
Lipid Lowering Therapies	**Statins**					
	Atorvastatin	No dose adjustment	Manufacturer recommends lowest dose (10 mg once daily) be used			Plasma concentrations are similar to those with normal renal function, but several cases of rhabdomyolysis reported in patients with renal insufficiency.
	Fluvastatin	No dose adjustment		Not recommended		Recommendation from manufacturer is based on lack of experience rather than renal excretion.
	Lovastatin	No dose adjustment		Use low dose (max dose 20 mg/day)		10% renal elimination. Doubling of plasma concentration in moderate to severe renal impairment.
	Pravastatin	No dose adjustment	Use lowest dose as precautionary measure			Lack of data. 20% renal elimination.
	Rosuvastatin	No dose adjustment		Use low dose (max dose 10 mg/day)		10% renal elimination.
	Simvastatin	No dose adjustment		Use low dose (max dose 10 mg/day)		13% renal elimination.
Neuropathy Therapies	**Anticonvulsants**					
	Gabapentin	Max 3600 mg/ day divided tid	Max 1400 mg/day divided bid	Max 700 mg/ day given once daily	Max 150-300 mg/day given once daily	Hemodialysis supplemental dosing required: 125-350 mg after each 4 hours of hemodialysis.
	Pregabalin	Max 600 mg/ day divided bid or tid	Max 300 mg/day divided bid or tid	Max 150 mg/ day given once daily or bid	Max 75 mg/ day given once daily	Hemodialysis supplemental dosing required.
Erectile Dysfunction Therapies	**Phosphodiesterase-5 (PDE-5) Inhibitors**					
	Sildenafil	No dose adjustment		Reduce starting dose to 25 mg		
	Tadalafil	No dose adjustment	10-20 mg (max frequency of alternate days and not more than 3 times per week)			2.5-5 mg once a day may be considered in CKD stage 3 but daily dosing is not recommended in CKD stage 4 and 5.