

Table 8.1—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

Medication	Efficacy*	Hypoglycemia	Weight Change	CV Effects		Cost	Oral/SQ	Renal Effects		Additional Considerations
				ASCVD	CHF			Progression of DKD	Dosing/Use considerations	
Metformin	High	No	Neutral (Potential for Modest Loss)	Potential Benefit	Neutral	Low	Oral	Neutral	Contraindicated with eGFR <30	<ul style="list-style-type: none"> Gastrointestinal side effects common (diarrhea, nausea) Potential for B12 deficiency
SGLT-2 Inhibitors	Intermediate	No	Loss	Benefit: canagliflozin, empagliflozin [†]	Benefit: canagliflozin, empagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	<ul style="list-style-type: none"> Canagliflozin: not recommended with eGFR <45 Dapagliflozin: not recommended with eGFR <60; contraindicated with eGFR <30 Empagliflozin: contraindicated with eGFR <30 	<ul style="list-style-type: none"> FDA Black Box: risk of amputation (canagliflozin) Risk of bone fractures (canagliflozin) DKA risk (all agents; rare in T2DM) Genitourinary infections Risk of volume depletion, hypotension ↓LDL cholesterol
				Neutral: lixisenatide, exenatide extended release	Neutral	High	SQ	Benefit: liraglutide	<ul style="list-style-type: none"> Exenatide: not indicated with eGFR <30 Lixisenatide: caution with eGFR <30 Increased risk of side effects in patients with renal impairment 	<ul style="list-style-type: none"> FDA Black Box: risk of thyroid C-cell tumors (liraglutide, albiglutide, dulaglutide, exenatide extended release) Gastrointestinal side effects common (nausea, vomiting, diarrhea) Injection site reactions ↑Acute pancreatitis risk
GLP-1 RAs	High	No	Loss	Neutral: lixisenatide, exenatide extended release	Neutral	High	High	Neutral	<ul style="list-style-type: none"> Renal dose adjustment required; can be used in renal impairment 	<ul style="list-style-type: none"> Potential risk of acute pancreatitis Joint pain
DPP-4 Inhibitors	Intermediate	No	Neutral	Neutral	Potential Risk: saxagliptin, alogliptin	High	Oral	Neutral	<ul style="list-style-type: none"> Renal dose adjustment required; can be used in renal impairment 	<ul style="list-style-type: none"> Potential risk of acute pancreatitis Joint pain
Thiazolidinediones	High	No	Gain	Potential Benefit: pioglitazone	Increased Risk	Low	Oral	Neutral	<ul style="list-style-type: none"> No dose adjustment required Generally not recommended in renal impairment due to fluid retention 	<ul style="list-style-type: none"> FDA Black Box: Congestive heart failure (pioglitazone, rosiglitazone) Fluid retention (edema; heart failure) Benefit in NASH Risk of bone fractures Bladder cancer (pioglitazone) ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd Generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	<ul style="list-style-type: none"> Glyburide: not recommended Glipizide & glimepiride: initiate conservatively to avoid hypoglycemia 	<ul style="list-style-type: none"> FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
							SQ	Neutral	<ul style="list-style-type: none"> Lower insulin doses required with a decrease in eGFR; treat per clinical response 	<ul style="list-style-type: none"> Injection site reactions Higher risk of hypoglycemia with human insulin (NH or premixed formulations) vs. analogs
Insulin	Highest	Yes	Gain	Neutral	Neutral	Low	SQ	Neutral	<ul style="list-style-type: none"> Lower insulin doses required with a decrease in eGFR; treat per clinical response 	<ul style="list-style-type: none"> Injection site reactions Higher risk of hypoglycemia with human insulin (NH or premixed formulations) vs. analogs
							High	SQ	Neutral	<ul style="list-style-type: none"> Lower insulin doses required with a decrease in eGFR; treat per clinical response

*See ref. 31 for description of efficacy. †FDA approved for CVD benefit. CVD, cardiovascular disease; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; NASH, nonalcoholic steatohepatitis; RAs, receptor agonists; SQ, subcutaneous; T2DM, type 2 diabetes.