At diagnosis of type 2 diabetes
Start lifestyle intervention (nutrition therapy and physical activity) +/- Metformin

A1C <8.5%	A1C ≥8.5%	Symptomatic hyperglycemia with metabolic decompensation
If not at glycemic target (2-3 mos)	Start metformin immediately Consider initial combination with another antihyperglycemic agent	Initiate insulin +/- metformin
Start/Increase metformin →	If not at glycemic targets	

Add another agent best suited to the individual by prioritizing patient characteristics:

PATIENT CHARACTERISTIC	CHOICE OF AGENT
Priority: Clinical Cardiovascular Disease →	SGLT2 inhibitor with demonstrated CV outcome benefit
• Degree of hyperglycemia • Risk of hypoglycemia • Overweight or obesity • Cardiovascular disease or multiple risk factors • Comorbidities (renal, CHF, hepatic) • Preferences & access to treatment	• Consider relative A1C lowering • Rare hypoglycemia • Weight loss or weight neutral • Effect on cardiovascular outcome • See therapeutic considerations, consider eGFR • See cost column; consider access

Add another class of agent best suited to the individual (classes listed in alphabetical order):

Class	Relative A1C Lowering	Hypo-glycemia	Weight	Effect in Cardiovascular Outcome Trial	Other therapeutic considerations	Cost
Alpha-glucosi-dase inhibitor (acarbose)	↓	Rare	Neutral to ↓		Improved postprandial control, GI side-effects	$$
Incretin agents: DPP-4 Inhibitors	↓↓	Rare	Neutral to ↓	Neutral (alo, saxa, sita)	Caution with saxagliptin in heart failure	$$$
GLP-1R agonists	↓↓ to ↓↓↓	Rare	↓↓	Neutral (lixi)	GI side effects	$$$$
Insulin	↓↓↓	Yes	↑↑	Neutral (glar)	No dose ceiling, flexible regimens	$-$$$$
Insulin secretagogue: Meglitinide	↓↓	Yes	↑		Less hypoglycemia in context of missed meals but usually requires TID to QID dosing	$$
Sulfonylurea	↓↓	Yes	↑		Gliclazide and glimepiride associated with less hypoglycemia than glyburide	$
SGLT2 inhibitors	↓↓ to ↓↓↓	Rare	↓↓	Superiority (empa in T2DM patients with clinical CVD)	Genital infections, UTI, hypotension, dose-related changes in LDL-C, caution with renal dysfunction and loop diuretics, dapagliflozin not to be used if bladder cancer, rare diabetic ketoacidosis (may occur with no hyperglycemia)	$$$
Thiazolidin-ediones	↓↓	Rare	↑↑	Neutral	CHF, edema, fractures, rare bladder cancer (pioglitazone), cardiovascular controversy (rosiglitazone), 6-12 weeks required for maximal effect	$$
Weight loss agent (orlistat)	↓	None	↓		GI side effects	$$$

alo=alogliptin; empa=empagliflozin; glar=glargine; lixi=lixisenatide; saxa=saxagliptin; sita=sitagliptin

If not at glycemic targets

• Add another agent from a different class • Add/Intensify insulin regimen

Make timely adjustments to attain target A1C within 3-6 months

L I F E S T Y L E

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