Type 2 Diabetes Management Algorithm – Supplement

Medication	A1c effect	Initial dose and titration	Benefits	Contraindications	Caution/Side Effects/Tips	Cost
Biguanide - ↓ hepatic glucose production and ↓ insulin resistance						
Metformin	↓ 1-2%	· 500mg 1 tab daily with meal → 1 tab BID → 2 tab BID, ↑ q1-2 wks · Max dose 1000mg BID or 850mg TID	· Unique mechanism · Weight neutral with possible weight loss · No risk of hypoglycemia with monotherapy	· eGFR < 30 · eGFR < 45, then consider risk/benefit and lower dose · Acute or unstable heart failure	· GI side effects – If so, consider reducing dose. Occasionally metformin ER is better tolerated. · B12 deficiency – check B12 level q 3 years · Very rarely associated with lactic acidosis	$
Sulfonylurea - ↑ glucose-***in***dependent insulin secretion (efficacy relies on functioning beta cells)						
Glipizide	↓ 1-2%	· 5mg daily before breakfast, ↑ 2.5-5mg q1-2 wks · Max dose 10mg before breakfast and dinner · Hold if skipping meal	· Highly effective	· Severe sulfa allergy · Type 1 DM	· Possible weight gain · Risk of hypoglycemia, esp in elderly or impaired renal/hepatic function (In CKD, glipizide has the least risk of hypoglycemia since cleared hepatically.) · If irregular meal access and at risk for severe hypoglycemia, consider repaglinide	$
GLP agonist - ↑ glucose-dependent insulin secretion, ↓ glucagon secretion, slow gastric emptying, ↑ satiety						
Liraglutide	↓ 0.5-1.5%	· 0.6mg daily → 1.2mg daily → 1.8mg daily. Uptitrate every 2-4 weeks as tolerated.	· Weight loss (~5kg) · In established ASCVD, with CV and nephropathy benefit · Low risk of hypoglycemia if used without insulin or sulfonylurea	· Hx or Fhx of medullary thyroid carcinoma or MEN2	· GI side effect common, but usually diminishes with time · If on insulin, may need to decrease doses · Possible increased risk of pancreatitis – avoid if hx of pancreatitis unless etiology resolved (ex. cholecystectomy) · Animal studies with association with medullary thyroid carcinoma, not demonstrated in humans	$$$
Semaglutide	↓ 0.5-1.5%	· 0.25mg weekly → 0.5mg weekly → 1mg weekly. Uptitrate every 2-4 weeks as tolerated.	· Weight loss (~5kg) · Low risk of hypoglycemia if used without insulin or sulfonylurea	*Same as liraglutide*	*Same as liraglutide* · If with diabetric retinopahy, consider slower titration to avoid rapid decline in A1c and retinal screening within 6 months to evaluate progression of retinopathy	$$$
Other GLP1-agonists: • Dulaglutide shown to have some CV benefit in patients with and without established ASCVD, but is currently only covered under some Medicare part D plans • Exenatide and exenatide ER have not been specifically studied to reduce CV risk in patients with establish ASCVD. However, they do have weight loss benefit. • Refer to Sharepoint GLP-1 agonist guide for more details						
SGLT2 inhibitor – blocks glucose reabsorption by kidney						
Empagliflozin	↓ 0.5-0.7%	· 10mg daily, ↑ to 25mg daily · Max dose 25mg daily	· In established ASCVD, with CV, decreased HF hospitalizations, and nephropathy benefit	· eGFR < 30 (see next column) · Ketosis-prone Type 2 DM or type 1	· Manufacturer label recommends not initiating agent if eGFR < 45. However, data suggests safety and benefit for eGFR 30-45 at 10mg or 25mg daily. If using in patient with eGFR < 45, recommend monitoring. Like ACEi/ARB,	$$$

			· Mild weight loss (2-3kg)	DM	at time of initiation there can be a drop in eGFR. If decrease progresses, then recommend discontinue agent. · Avoid if prone to UTI or GU infections, FDA alert on necrotizing fascitis · Risk of euglycemic DKA · Caution if hypotensive · Canagliflozin demonstrated to have an increased risk of amputation and fracture, not yet clear if this is a class effect. Recommend regular foot exam.	
Canagliflozin	↓ 0.5-0.7%	· 100mg daily, ↑ to 300mg daily · Max dose 300mg daily	· In CKD with proteinuria, with nephropathy and CV benefit · In established ASCVD, with CV, decrease HF hospitalizations, and nephropathy benefit	· eGFR < 30 (see next column) · Ketosis-prone Type 2 DM or type 1 DM	**· FDA black box warning on increased risk of amputation.** Avoid if history of or has risk of ulcers/amputations and recommend regular foot exam. · Possible increase in fracture risk · Manufacturer label recommends not initiating agent if eGFR < 45. However, recent data showed safety and benefit for eGFR 30-45 at 100mg daily. If using in patient with eGFR < 45, recommend monitoring. Like ACEi/ARB, at time of initiation there can be a drop in eGFR. If decrease progresses, then discontinue agent. · Avoid if prone to UTI or GU infections, FDA alert on necrotizing fascitis · Risk of euglycemic DKA · Caution if hypotensive	$$$
Dapagliflozin	↓ 0.5-0.7%	· 5mg daily, ↑ to 10mg daily · Max dose 10mg daily	· In established ASCVD, with CV, decrease HF hospitalizations, and nephropathy benefit · Mild weight loss (2-3kg)	· eGFR < 45 · Ketosis-prone Type 2 DM or type 1 DM	· Avoid if prone to UTI or GU infections · Risk of euglycemic DKA · Caution if hypotensive · Canagliflozin demonstrated to have an increased risk of amputation and fracture, not yet clear if this is a class effect. Recommend regular foot exam. · Unclear association with bladder cancer	$$$
Thiazolidinediones - ↑ insulin sensitivity						
Pioglitazone	↓ 0.5-1.4%	· 15 mg daily, ↑ by 15 mg q2-3 mo · Max dose 45 mg daily	· Benefit in NASH · No risk of hypoglycemia with monotherapy	· CHF · Active liver disease or ALT > 2.5x ULN	· Weight gain, fluid retention · May be associated with ↑ fracture risk and bladder CA · May take 6-12 weeks to see max effect	$$
Meglitinide - ↑ insulin secretion with rapid onset and short duration of action						
Repaglinide	↓0.5-1.5%	· 0.5 to 4mg with each meal, titrate based off of postprandial glucoses	· Useful in pts with irregular meal patterns		· Requires frequent dosing (with meals) · Risk of hypoglycemia – hold if not eating carbs · Can be used in CKD	$$
Alpha-glucosidase inhibitor – slows intestinal digestion and absorption of carbohydrates						
Acarbose	↓ 0.5-	· 25 mg TID with first	· Weight neutral	· Known GI issues	· Flatulence, diarrhea, abdominal pain – generally	$$

	0.8%	bit of meal, ↑ by 25-50 mg per meal q4-8 wks as needed to achieve goal blood sugars and to minimize GI side effects. · Max dose 50 mg TID for pt < 60 kg, or 100 mg TID for pt > 60 kg		with digestion/absorption (ex. IBD), cirrhosis	diminishes over time · While acarbose does not cause hypoglycemia, if pt develops hypoglycemia, treat with oral glucose tabs (dextrose). Acarbose inhibits sucrose absorption. · Check AST/ALT q3 mo in first year – elevated LFTs have been observed, dose-related · Not studied in Cr > 2.0 mg/dL	
DPP4 inhibitor - ↑ glucose-dependent insulin secretion, ↓ glucagon secretion						
Saxagliptin	↓ 0.5-0.8%	· 2.5 to 5mg daily	· Weight neutral · Low risk of hypoglycemia	· Dose reduction for eGFR < 45	· Joint pain, nasopharyngitis · Associated with pancreatitis	$$$
Sitagliptin		· 25 to 100mg daily		· Dose reduction for eGFR < 45	· Associated with increased CHF admission · Joint pain, nasopharyngitis · Associated with pancreatitis	$$$
Linagliptin		· 5mg daily			· Does not require dose reduction in CKD · Potential risk of pancreatitis	$$$
Alogliptin		· 6.25 to 25mg daily		· Dose reduction for eGFR < 60	· Nasopharyngitis	$$$