Type 2 Diabetes Management Algorithm – Supplement

| Medication | A1c effect | Initial dose and titration | Benefits | Contraindications | Caution/Side Effects/Tips | Cost |
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| 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<br>· Max dose 1000mg BID or 850mg TID | · Unique mechanism<br>· Weight neutral with possible weight loss<br>· No risk of hypoglycemia with monotherapy | · eGFR < 30<br>· eGFR < 45, then consider risk/benefit and lower dose<br>· Acute or unstable heart failure | · GI side effects – If so, consider reducing dose. Occasionally metformin ER is better tolerated.<br>· B12 deficiency – check B12 level q 3 years<br>· 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<br>· Max dose 10mg before breakfast and dinner<br>· Hold if skipping meal | · Highly effective | · Severe sulfa allergy<br>· Type 1 DM | · Possible weight gain<br>· Risk of hypoglycemia, esp in elderly or impaired renal/hepatic function (In CKD, glipizide has the least risk of hypoglycemia since cleared hepatically.)<br>· 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)<br>· In established ASCVD, with CV and nephropathy benefit<br>· 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<br>· If on insulin, may need to decrease doses<br>· Possible increased risk of pancreatitis – avoid if hx of pancreatitis unless etiology resolved (ex. cholecystectomy)<br>· Animal studies with association with medullary thyroid carcinoma, not demonstrated in humans | $$$ |
| Semaglutide | ↓ 0.5-1.5% | · 0.25mg weekly → 0.5mg weekly → 1mg weekly. Uptitrate every 2-4 weeks as tolerated. | · Weight loss (~5kg)<br>· Low risk of hypoglycemia if used without insulin or sulfonylurea | *Same as liraglutide* | *Same as liraglutide*<br>· If with diabetric retinopahy, consider slower titration to avoid rapid decline in A1c and retinal screening within 6 months to evaluate progression of retinopathy | $$$ |
| Other GLP1-agonists:<br>• 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<br>• 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.<br>• 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<br>· Max dose 25mg daily | · In established ASCVD, with CV, decreased HF hospitalizations, and nephropathy benefit | · eGFR < 30 (see next column)<br>· 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, | $$$ |

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| | | | · Mild weight loss (2-3kg) | DM | at time of initiation there can be a drop in eGFR. If decrease progresses, then recommend discontinue agent.<br>· Avoid if prone to UTI or GU infections, FDA alert on necrotizing fascitis<br>· Risk of euglycemic DKA<br>· Caution if hypotensive<br>· 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<br>· Max dose 300mg daily | · In CKD with proteinuria, with nephropathy and CV benefit<br>· In established ASCVD, with CV, decrease HF hospitalizations, and nephropathy benefit | · eGFR < 30 (see next column)<br>· 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.<br>· Possible increase in fracture risk<br>· 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.<br>· Avoid if prone to UTI or GU infections, FDA alert on necrotizing fascitis<br>· Risk of euglycemic DKA<br>· Caution if hypotensive | $$$ |
| Dapagliflozin | ↓ 0.5-0.7% | · 5mg daily, ↑ to 10mg daily<br>· Max dose 10mg daily | · In established ASCVD, with CV, decrease HF hospitalizations, and nephropathy benefit<br>· Mild weight loss (2-3kg) | · eGFR < 45<br>· Ketosis-prone Type 2 DM or type 1 DM | · Avoid if prone to UTI or GU infections<br>· Risk of euglycemic DKA<br>· Caution if hypotensive<br>· Canagliflozin demonstrated to have an increased risk of amputation and fracture, not yet clear if this is a class effect. Recommend regular foot exam.<br>· Unclear association with bladder cancer | $$$ |
| Thiazolidinediones - ↑ insulin sensitivity | | | | | | |
| Pioglitazone | ↓ 0.5-1.4% | · 15 mg daily, ↑ by 15 mg q2-3 mo<br>· Max dose 45 mg daily | · Benefit in NASH<br>· No risk of hypoglycemia with monotherapy | · CHF<br>· Active liver disease or ALT > 2.5x ULN | · Weight gain, fluid retention<br>· May be associated with ↑ fracture risk and bladder CA<br>· May take 6-12 weeks to see max effect | $$ |
| Meglitinide - ↑ insulin secretion with rapid onset and short duration of action | | | | | | |
| Repaglinide | ↓0.5-1.5% | · 0.5 to 4mg with each meal, titrate based off of postprandial glucoses | · Useful in pts with irregular meal patterns | | · Requires frequent dosing (with meals)<br>· Risk of hypoglycemia – hold if not eating carbs<br>· Can be used in CKD | $$ |
| 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 | $$ |

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| | 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.<br>· 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<br>· While acarbose does not cause hypoglycemia, if pt develops hypoglycemia, treat with oral glucose tabs (dextrose). Acarbose inhibits sucrose absorption.<br>· Check AST/ALT q3 mo in first year – elevated LFTs have been observed, dose-related<br>· 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<br>· Low risk of hypoglycemia | · Dose reduction for eGFR < 45 | · Joint pain, nasopharyngitis<br>· Associated with pancreatitis | $$$ |
| Sitagliptin | | · 25 to 100mg daily | | · Dose reduction for eGFR < 45 | · Associated with increased CHF admission<br>· Joint pain, nasopharyngitis<br>· Associated with pancreatitis | $$$ |
| Linagliptin | | · 5mg daily | | | · Does not require dose reduction in CKD<br>· Potential risk of pancreatitis | $$$ |
| Alogliptin | | · 6.25 to 25mg daily | | · Dose reduction for eGFR < 60 | · Nasopharyngitis | $$$ |