Glucose Management in Type 2 Diabetes Medications

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Medications on the IHS National Core Formulary are in BOLD and highlighted in this algorithm. Please consult a complete prescribing reference for more detailed information. This is not a complete reference for non-insulin diabetes medications. No endorsement of specific products is implied.

Metformin

A biguanide that reduces hepatic glucose production

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dosing
Metformin	500 mg/day	2000 mg/day (BID or TID)	1-2%	+ / -	Max dose 1000mg/d if eGFR 30–60. Do not use if eGFR <30

Additional benefits: Neutral effect on weight, no hypoglycemia
Side effects: Abdominal bloating and diarrhea; B12 deficiency with long-term use, monitor and supplement with vitamin B12, as needed
Comments: Risk for lactic acidosis (rare serious event); FDA-approved for treatment of type 2 diabetes in children aged 10 years and older

Glucagon-like Peptide-1 Receptor Agonists (GLP-1 RA)

Potentiate glucose-dependent increase in insulin levels and decrease in glucagon levels.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dose Adjustment
Semaglutide (*Ozempic*)	0.25 mg SC/wk	Increase monthly to 2 mg SC/week, as needed	1-2 to >2%	+ / -	None

Other GLP-1RA: Dulaglutide *(Trulicity),* exenatide *(Byetta) and* exenatide ER *(Bydureon BCise),* liraglutide *(Victoza),* lixisenatide *(Adlyxin),* and oral semaglutide *(Rybelsus).* Details for dosing, renal adjustments, and additional indications, such as CVD, CKD, or CHF benefit, are available in individual product prescribing information.
Additional benefits: Reduce appetite, weight loss, no hypoglycemia
Side effects: Nausea and vomiting, abdominal pain, constipation, diarrhea, decreased appetite, gall bladder disease
Contraindications: Personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2
Comments: Risk for thyroid C-cell tumors, pancreatitis, ileus (intestinal blockage), and acute kidney injury; FDA-approved for treatment of type 2 diabetes in children aged 10 years and older (liraglutide and exenatide ER)

Glucose-dependent Insulinotropic Polypeptide (GIP)/GLP-1 Receptor Agonists

Potentiate glucose-dependent increase in insulin levels and decrease in glucagon levels, as well as, increased insulin sensitivity.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dose Adjustment
Tirzepatide (*Mounjaro*)	2.5 mg SC/wk	Increase dose by 2.5 mg a month to 15 mg SC/wk as needed	1-2 to >2%	- / -	None

Additional benefits: Reduce appetite, weight loss, no hypoglycemia
Side effects: Nausea and vomiting, abdominal pain, constipation, diarrhea, gall bladder disease
Contraindications: Personal/family history: medullary thyroid cancer, multiple endocrine neoplasia type 2

*** Note:** CVD, CHF, CKD benefit (+/-) designation is based on clinical evidence and/or FDA approved indication

Sodium-glucose Cotransporter 2 Inhibitors (SGLT2i)

Inhibit SGLT-2 in the kidneys to decrease glucose and sodium reabsorption and increase glycosuria.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	CHF * Benefit	Renal Dosing
Empagliflozin (*Jardiance*)	10 mg/day	25 mg/day	0.5-1.5%	+ / -	+	eGFR <30: avoid use for glycemic control

Other SGLT-2i: Bexagliflozin *(Brenzavvy),* canagliflozin *(Invokana),* dapagliflozin *(Farxiga),* ertugliflozin *(Steglatro), and* sotagliflozin *(Inpefa).* Details for dosing, renal adjustments, and additional indications, such as CVD, CKD, or CHF benefit, are available in individual product prescribing information.
Additional benefits: Decreased systolic blood pressure, weight loss, no hypoglycemia
Side effects: Genital mycotic infections, dehydration, increased urinary frequency.
Comments: Risk for diabetic ketoacidosis and Fournier's Disease (rare serious events). Empagliflozin is FDA-approved for treatment of type 2 diabetes in children aged 10 years and older.

Dipeptidyl Peptidase-4 Inhibitors (DPP-4i)

Increase endogenous GLP-1 levels resulting in increased glucose-dependent insulin secretion and glucagon suppression.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dosing
Alogliptin (*Nesina*)	25 mg/day (max dose)		0.5-1.5%	- / -	eGFR 30-60: max dose 12.5 mg/day dialysis: max dose 6.25 mg/day

Other DPP-4i: Linagliptin *(Tradjenta),* saxagliptin *(Onglyza), and* sitagliptin *(Januvia).* Details for dosing, renal adjustments, and additional indications are available in individual product prescribing information.
Additional benefits: No hypoglycemia, neutral weight effect, once a day medication
Side effects: Mild nasopharyngitis, increased heart failure hospitalization was observed in clinical trials of saxagliptin and alogliptin.

Sulfonylureas

Stimulate insulin secretion from β-cells.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dosing
Glipizide *Glipizide ER*	2.5-5 mg/day 2.5-10 mg/day	20 mg bid 20 mg/day	1-2%	- / -	Half max dose in renal failure

Other sulfonylureas: Glimepiride and glyburide. Details for dosing, renal adjustments, and additional Indications are available in individual product prescribing information.
Side effects: Weight gain, hypoglycemia, especially with glyburide

Thiazolidinedione (TZD)

Reduces insulin resistance through modulation of insulin sensitive genes.

	Starting Dose	Titrate up to	A1C Reduction	CVD/CKD * Benefit	Renal Dose Adjustment
Pioglitazone	15 mg/day	30-45 mg/day	1-2%	+ / -	None

Side effects: Weight gain and edema, risk for heart failure hospitalization
Comments: Glycemic effect may take longer than one month to be fully appreciated.