

Glucose Management in Type 2 Diabetes Medications

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

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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
Sitagliptin (Januvia)	100 mg/day (max dose)		0.5-1.5%	- / -	eGFR 30-44: max dose 50 mg/day eGFR <30 or dialysis: max dose 25 mg/day

Other DPP-4i: Alogliptin (*Nesina*), linagliptin (*Tradjenta*), and saxagliptin (*Onglyza*). 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.