

Please Note: This algorithm is **not** intended for treatment and target selection in children or in women who are or could become pregnant.

Step 1: Determine Individualized Glycemic Target

A1C Target Range: Select based on age, duration of diabetes, patient preference, comorbidities, hypoglycemia risk, and other factors.

Major Comorbidity	Microvascular Complications		
	Absent or Mild	Moderate	Advanced
Absent (and/or >10-15 years of life expectancy)	6.0-7.0%	7.0-8.0%	7.5-8.5%
Present (and/or 5-10 years of life expectancy)	7.0-8.0%	7.5-8.5%	7.5-8.5%
Marked (and/or <5 years of life expectancy)	8.0-9.0%	8.0-9.0%	8.0-9.0%

Major comorbidity includes but is not limited to significant CVD; recent stroke; life-threatening malignancy; or severe CKD, COPD, or chronic liver disease.

Microvascular disease: retinopathy, neuropathy, or CKD.

Adapted from the [VA/DoD Management of Diabetes Mellitus Guideline](#)



Step 2: Initiate Medication Therapy

If significant weight loss or ketonuria, use **insulin** (hospitalize if acidotic).

Otherwise:

Start **metformin** if A1C above patient's target but <9%.

Start metformin **and** a second medication if A1C ≥9% (see Step 3).



Step 3: If A1C above patient's target range, increase dosage(s) and/or add another medication

Select additional medication(s) based on formulary options, side effects, comorbidities, cost, medication regimen complexity, and patient preference.

Medication	Weight	Risk of		Cost
		A1C	Hypoglycemia	
Metformin	- / ↓	↓↓	-	↑
DPP-4 Inhibitor	-	↓	-	↑↑
GLP-1 Receptor Agonist	↓↓	↓↓	-	↑↑↑
Insulin	↑↑ / ↑↑↑	↓↓↓	↑↑↑	↑↑
SGLT2 Inhibitor	- / ↓	↓	-	↑↑↑
Sulfonylurea	↑↑	↓↓	↑↑	↑
Thiazolidinedione	↑	↓↓	-	↑↑

Do not use GLP-1 Receptor Agonists and DPP-4 inhibitors together as no A1C benefit.

Metformin

Start 500mg daily with meals and increase no faster than 500mg/day each week.

If GI symptoms occur, may increase more slowly.

Max dose: Regular release tablets: 2,550mg divided BID or TID.

XR tablets: 2,000mg daily or divided BID.

Monitor and supplement vitamin B12 as needed with long term use.

Discontinue if eGFR <30mL/min/1.73m².

Warning: May cause lactic acidosis.

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

Saxagliptin (Onglyza®) Dose: 2.5-5mg daily. Use 2.5mg if eGFR ≤50mL/min/1.73m².

May increase risk of heart failure, especially in patients with heart or kidney disease.

Linagliptin (Tradjenta®) 5mg daily.

Sitagliptin (Januvia®) 100mg daily (reduce dose if eGFR ≤50mL/min/1.73m²).

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Exenatide (Byetta®) Start 5mcg BID SC in thigh, abdomen, or upper arm.

May increase to 10mcg BID after 1 month. Administer within 60 minutes before meals.

Exenatide ER (Bydureon®) Start 2mg SC weekly.

For *Exenatide/Exenatide ER*: See prescribing reference when eGFR <60ml/min/1.73m².

Liraglutide (Victoza®) Start 0.6mg SC daily in thigh, abdomen, or upper arm.

Increase to 1.2mg daily in 1 week. May increase to 1.8mg daily.

Pancreatitis and acute kidney injury have been reported. GI side effects common.

Warning: May increase risk of thyroid tumor.

Insulin - See Insulin algorithm.

Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors

Canagliflozin (Invokana®) Start 100mg daily before first meal. May increase to 300mg daily.

Warning: May increase risk of lower limb amputations.

Dapagliflozin (Farxiga®) Start 5mg every morning. May increase to 10mg daily.

Empagliflozin (Jardiance®) Start 10mg daily. May increase to 25mg daily.

May cause volume depletion, orthostatic hypotension, genital fungal infections, and UTI.

For all SGLT2 Inhibitors: See prescribing reference when eGFR <60ml/min/1.73m².

Sulfonylureas

Glipizide Start 2.5-5mg daily - max 20mg BID. ER formulation dosed 5-20mg daily.

Glimepiride Start 1-2mg daily - max 8mg daily.

May cause hypoglycemia, weight gain.

Thiazolidinedione (TZD)

Pioglitazone (Actos®) Start 15mg daily; may increase to 30-45mg daily.

Max A1C changes may take up to 12 weeks to occur.

May increase risk of bone fracture. Do not use in patients with bladder cancer.

Check LFTs before starting. May cause weight gain.

Warning: Increased risk of heart failure.

Medications on the **IHS National Core Formulary** are in **BOLD** above.

This is a summary of the most commonly ordered non-insulin diabetes medications and drug classes from the IHS National Supply Service Center. No endorsement of specific products is implied. Please consult a complete prescribing reference for more detailed information.