2026 Standards of Care for Diabetes

San Francisco Health Plan℠

Non-Insulin Medication Treatment for DM II

The 2023 American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) and 2026 American Diabetes Association (ADA) provided updated recommendations for pharmacologic treatment of diabetes. Both guidelines **recommend early incorporation of agents with proven cardiovascular, renal, and weight loss benefit**, including a sodium-glucose cotransporter 2 inhibitor (SGLT-2i) or glucagon-like peptide-1 receptor agonist (GLP-1 RA), in addition to or independent of metformin based on comorbidity profile.

Therapy selection is now comorbidity-driven, in which medication selection is guided by the presence of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), heart failure (HF), and obesity, rather than glycemic targets alone.

Other oral medications like **dipeptidyl peptidase-4 inhibitors, thiazolidinediones, and sulfonylureas** are still options for treatment, but have been **de-emphasized** in these new guidelines. These classes **remain as options when cost or tolerability limit use of preferred therapies,** but their routine use is de-emphasized due to lower efficacy, lack of CV/renal benefit, and greater risk of hypoglycemia or weight gain.

1st Line treatments
AACE/ACE Complications-Centric and Glucose-Centric DM2 Management Algorithm

Clinical Scenario	Preferred 1st-line Agent
ASCVD or High Risk	GLP-1 RA or SGLT2i
Heart Failure	SGLT2i
Stroke/TIA	GLP-1 RA or pioglitazone
CKD	SGLT2i or GLP-1 RA
Overweight or Obesity	Metformin or GLP-1 RA or GIP/GLP-1 RA or SGLT2i
Hypoglycemia Risk	Metformin or GLP-1 RA or GIP/GLP-1 RA or SGLT2i

- Order of medication suggests hierarchy for selection
- Combination therapy should be initiated earlier when A1C ≥ 7.5% or when CKM comorbidities are present. GLP-1 RA, dual incretin therapy, or SGLT-2 inhibitors may be used independent of metformin when clinically indicated.

Class & Drugs	Efficacy (A1C reduction)	Cardiovascular Impact	Renal Impact	Weight & MASH Impact	Additional Safety Information
Biguanide • metformin (Glucophage®)¥	High (1–2%)	Potential ASCVD benefit HF neutral	Contraindicated with eGFR <30 mL/min/1.73 m^2	Neutral weight benefit (potential for modest loss) MASH neutral	GI side effects common (diarrhea, nausea, abdominal cramping); can be reduced with titration and use of ER form Potential B12 deficiency and lactic acidosis
Glucagon-like Peptide-1 Receptor Agonist (GLP-1 RA) • liraglutide (Victoza®)¥ • semaglutide (Ozempic® SQ, Rybelsus® PO)¥ • dulaglutide (Trulicity®)¥ • exenatide (Bydureon®, Byetta®)¥ • lixisenatide (Adlyxin®)	High (1–1.5%)	ASCVD benefit: dulaglutide, liraglutide, semaglutide HF neutral	CKD progression benefit: semaglutide (SQ) Benefit for renal end points in CVOTs (Cardiovascular Outcome Trials), driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ)	Intermediate to very high weight loss Potential MASH benefit	GI side effects common (nausea, vomiting, diarrhea, abdominal pain); can be reduced with titration Injection site reactions Potential for pancreatitis; use caution **Black Box Warning**: risk of thyroid C-cell tumors, contraindicated in family history of medullary thyroid carcinoma (MTC)
Dual Glucose-dependent Insulinotropic Polypeptide receptor and Glucagon-like Peptide-1 Receptor Agonist (GIP/GLP-1 RA) • tirzepatide (Mounjaro®)¥	Very High (up to 2.5%)	Under investigation	Under investigation	Very high weight loss Potential MASH benefit	GI side effects similar to GLP-1 Ras **Black Box Warning:** risk of thyroid C-cell tumors, contraindicated in family history of MTC
Sodium Glucose Cotransporter 2 Inhibitor (SGLT2i) • empagliflozin (Jardiance®)¥ • canagliflozin (Invokana®)¥ • dapagliflozin (Farxiga®)¥ • ertugliflozin (Steglatro®)	Intermediate (0.5 1%)	ASCVD benefit: canagliflozin, empagliflozin HF benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	CKD progression benefit: canagliflozin, dapagliflozin, empagliflozin	Intermediate weight loss Unknown MASH effect	Risk of bone fractures (canagliflozin only), genitourinary infections, DKA, volume depletion, hypotension, Fournier's gangrene

¥ Available on the Medi-Cal CDL without TAR

References

1. American Diabetes Association. Standards of Medical Care in Diabetes – 2026. Diabetes Care. 2026;49(Suppl. 1).
2. Garber AJ et al. AACE Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. Endocr Pract. 2023;29(4):305–340.
3. ADA. Summary of Revisions: Standards of Care in Diabetes – 2026

001923C 0126