



Non-Insulin Medication Treatment for DM II

The American Association of Clinical Endocrinologists and American College of Endocrinology (AAACE/ACE) and American Diabetes Association (ADA) provided updated recommendations for pharmacologic treatment of diabetes in 2020. Both guidelines recommend adding either a Sodium-Glucose Cotransporter 2 Inhibitor (SGLT-2i) or Glucagon-like Peptide 1 Receptor Agonist (GLP-1 RA) to Metformin as a second-line agent due to their demonstrated cardiovascular disease benefit.

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.

Further information on these new guidelines is available at the DHCS DUR website under "Educational Articles."

<https://files.medi-cal.ca.gov/pubsdoco/dur/edarticles.aspx>

1st Line treatments AAACE/ACE Comprehensive DM2 Management Algorithm

Initial A1C < 7.5%: Monotherapy

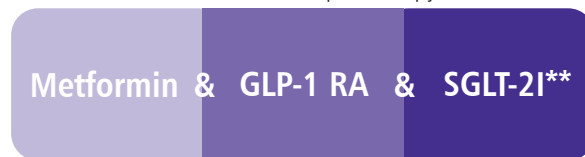


* Consider adding GLP-1 RA or SGLT-2i if indicated for cardiovascular risk.

Initial A1C > 7.5% OR Goal Not Met: Dual Therapy



Goal Not Met: Triple Therapy



** For symptomatic patients with A1C > 9%, insulin is recommended.

Class & Drugs	Efficacy (A1C Reduction)	Cardiovascular Impact	Additional Safety Information
Biguanide • Metformin (Glucophage®)‡	High (1-2%)	Potential ASCVD Benefit HF 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®) Rybelsus® • Dulaglutide (Trulicity®)‡ • Exenatide (Bydureon®, Byetta®)‡ • Lixisenatide (Adlyxin®)	High (1-1.5%) Liraglutide > Lixisenatide	ASCVD Benefit: Liraglutide, Semaglutide, Dulaglutide HF Neutral	GI side effects common (nausea, vomiting, diarrhea, abdominal pain); can be reduced with titration Injection site reactions. Potential for pancreatitis; use caution. Contraindicated in h/o of Multiple Endocrine Neoplasia Syndrome Type 2 (MEN2). Black Box Warning: Risk of thyroid C-cell tumors, contraindicated in family history of Medullary Thyroid Carcinoma (MTC).
Sodium Glucose Cotransporter 2 Inhibitor (SGLT2i) • Empagliflozin (Jardiance®)‡ • Canagliflozin (Invokana®) • Dapagliflozin (Farxiga®)‡ • Ertugliflozin (Steglatro®)	Intermediate (0.5-1%) Superior to DPP-4i	ASCVD Benefit: Empagliflozin, Canagliflozin HF Benefit: Empagliflozin, Canagliflozin, Dapagliflozin	Risk of Bone Fractures (Canagliflozin only), Genitourinary Infections, DKA, Volume Depletion, Hypotension, Fournier's gangrene. Risk of Amputation (Canagliflozin); Black Box Warning recently removed.***

‡ Available on the Medi-Cal CDL without TAR

*** In August of 2020, the FDA removed the Black Box Warning for Canagliflozin due to new safety information that demonstrates that while risk for amputation is increased with Canagliflozin, it is lower than previously described.

References:

1. American Diabetes Association. Standards of Medical Care in Diabetes – 2020. Diabetes Care. 2020 Jan; 43 (Supplement 1): S1-S212.
Available at: https://care.diabetesjournals.org/content/43/Supplement_1. Accessed: August 12, 2020.
2. American Association of Clinical Endocrinologists and American College of Endocrinology. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm – 2020 Executive Summary. Endocr Pract. 2020;26 (No. 1).
Available at: <https://www.aace.com/pdfs/diabetes/algorithm-exec-summary.pdf>. Accessed: September 16, 2020
3. FDA. FDA removes Boxed Warning about risk of leg and foot amputations for the diabetes medicine Canagliflozin (Invokana, Invokamet, Invokamet XR). August 26, 2020. Drug Safety and Availability.
Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-removes-boxed-warning-about-risk-leg-and-foot-amputations-diabetes-medicine-canagliflozin>. Accessed: September 16, 2020.