Evidence Summary: Cardiovascular Safety and Risk Reduction

	DPP-4 Inhibitors	GLP-1 Receptor Agonists	SGLT-2 Inhibitors	Reference
T2DM with ASCVD[*] for added glycemic control	ALL	ALL	ALL	1
T2DM with ASCVD[*] for ASCVD risk reduction, regardless of glycemic control	None	**Dulaglutide** **Liraglutide** **Semaglutide (SQ only)**	**Empagliflozin** **Canagliflozin**	2 – 4
T2DM with heart failure for added glycemic control	Sitagliptin Linagliptin	ALL	ALL	3
T2DM with heart failure for reduced hospitalizations, regardless of glycemic control	None	None	**Empagliflozin**[$] **Dapagliflozin**[$] Canagliflozin Ertugliflozin	2, 3
Improved heart failure outcomes, regardless of presence of T2DM	None	None	**Empagliflozin** **Dapagliflozin**	3,5
T2DM with CKD for added glycemic control	ALL	ALL	ALL	2 – 4
T2DM with CKD for improved CKD outcomes, regardless of glycemic control	None	**Dulaglutide**[**] Liraglutide[**] Semaglutide (subq only)[**]	Empagliflozin **Dapagliflozin** **Canagliflozin**	2,4
Improved CKD outcomes, regardless of presence of T2DM	None	None	**Dapagliflozin**	6
Usual Dose[†]	Alogliptin 25 mg daily Linagliptin 5mg daily Saxagliptin 2.5 – 5 mg daily Sitagliptin 100 mg daily	Dulaglutide 1.5 – 4.5 mg SQ weekly Liraglutide 1.2 – 1.8 mg SQ daily Semaglutide 0.5 – 1 mg SQ weekly Semaglutide 7 – 14 mg orally daily Lixisenatide 10 - 20 mcg SQ daily Exenatide ER2 mg SQ weekly	Canagliflozin 300 mg daily Dapagliflozin 10 mg daily Empagliflozin 25 mg daily Ertugliflozin 15 mg daily	
Renal Dose Adjustment Required	Alogloptin Saxagliptin	<u>CrCl ≤ 30 mL/min</u> AVOID: Exenatide, Lixisenatide	All require renal dose adjustment	

	Sitagliptin		Generally contraindicated if eGFR ≤ 30 mL/min or ESRD	

Notes: Albiglutide not included due to lack of availability in United States. [†]Oral dosage form unless designated otherwise. [*]Or high risk for ASCVD; [$]ADA recommends only empa and dapa; [**]ADA recommends GLP1 with ASCVD benefit only if unable to use SGLT2 inhibitor; **BOLDED: Potentially preferred within category, due to stronger available evidence** CrCl = creatinine clearance; DPP-4 = dipeptidyl peptidase-4; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; GLP-1 = glucagon-like-1 protein; mcg = microgram; mg = milligram; mL/min = milliliters per minute; SGLT-2 = sodium-glucose cotransporter-2; SQ = subcutaneous

References

1. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;74:e177–232.
2. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes – 2021. Diabetes Care 2021;44(Suppl. 1):S111–S124
3. Das SR, Everett BM, Birtcher KK, et al. 2020 Expert consensus decision pathway on novel therapies for cardiovascular risk reduction in patients with type 2 diabetes: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2020;76:1117–45.
4. Garber AJ, Handelsman Y, Grunberger G, et al. 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;26:107-39.
5. Writing Committee, Maddox TM, Januzzi JL Jr, Allen LA, Breathett K, Butler J, Davis LL, Fonarow GC, Ibrahim NE, Lindenfeld J, Masoudi FA, Motiwala SR, Oliveros E, Patterson JH, Walsh MN, Wasserman A, Yancy CW, Youmans QR. 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021 Feb 16;77(6):772-810. doi: 10.1016/j.jacc.2020.11.022. Epub 2021 Jan 11.
6. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med 2020;383:1436-46.