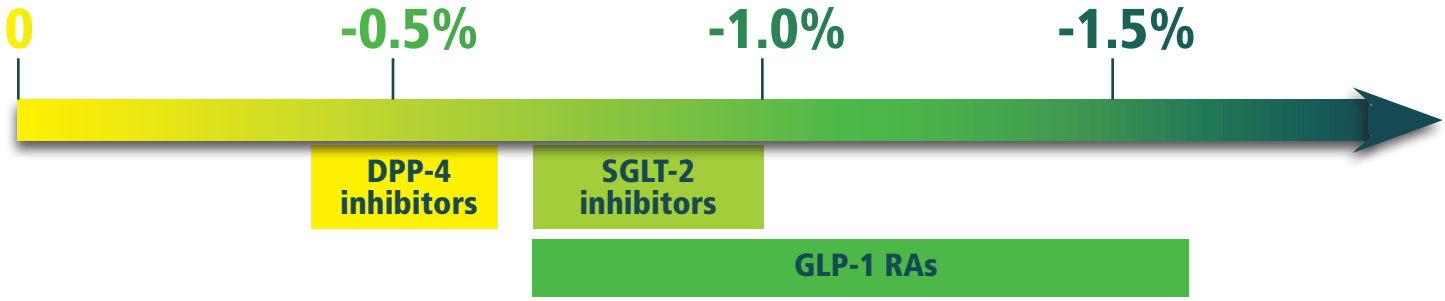
Factors to Consider When Incorporating New Therapies Into a Patient's Antihyperglycemic Regimen

Expected HbA1c Reduction for New Antihyperglycemic Medications*



Class and Available Compounds	Mechanism of Action[1,2]	Advantages[1,2]	Disadvantages[1,2]
DPP-4 Inhibitors • Alogliptin[3] • Linagliptin[4] • Saxagliptin[5] • Sitagliptin[6]	Inhibits DPP-4 activity, which increases postprandial active incretin (GLP-1, GIP) concentrations, leading to increased insulin secretion and decreased glucagon secretion	No hypoglycemia Weight neutral Well tolerated	Acute pancreatitis risk? – use caution in patients with history of pancreatitis Increased heart-failure hospitalizations with SAXA? – use caution in patients with preexisting heart failure Angioedema/urticaria and other immune-mediated dermatologic effects Severe joint pain
GLP-1 RAs Once daily • Exenatide[7] • Liraglutide[8] Once weekly • Exenatide extended release[9] • Albiglutide[10] • Dulaglutide[11]	Activates GLP-1 receptors leading to increased insulin secretion, decreased glucagon secretion, slowed gastric emptying, and increased satiety	No hypoglycemia Weight loss ranging from approximately -1.4 kg to -2.9 kg (-3 lb to -6.4 lb)* Associated with reduction in some CV risk factors Reduced postprandial glucose excursions	Gastrointestinal adverse effects (nausea, vomiting, diarrhea) Increased heart rate Acute pancreatitis risk? – use caution in patients with history of pancreatitis C-cell hyperplasia/medullary thyroid tumors observed in animals Injectable therapy with training requirements
SGLT-2 Inhibitors • Canagliflozin[12] • Dapagliflozin[13] • Empagliflozin[14]	Inhibits SGLT-2 in the proximal nephron, which blocks glucose reabsorption by the kidney and increases glycosuria	No hypoglycemia Weight loss ranging from approximately -2.6 kg to -3.9 kg (5.7 lb to 8.6 lb)* Decreased blood pressure Effective at all stages of T2DM	Genitourinary infections Polyuria Volume depletion/hypotension/dizziness – use caution in elderly patients, patients already on a diuretic, or patients with tenuous intravascular volume status Increased LDL cholesterol Increased creatinine (transient effect) Risk for diabetic ketoacidosis Increased bone fracture with CANA?

*As reported from monotherapy studies comparing each agent to placebo. Length of each monotherapy study varied among 24, 26, and 52 weeks.[3-14]

References

1. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2015;38(1):140-149.
2. Inzucchi SE, Bergenstal RM, Buse JB, et al; American Diabetes Association (ADA); European Association for the Study of Diabetes (EASD). Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2012;35(6):1364-1379.
3. US FDA CDER. Alogliptin NDA 022271. Label 1/25/2013.
4. US FDA CDER. Linagliptin NDA 201280. Label 7/28/2015.
5. US FDA CDER. Saxagliptin NDA 022350. Label 5/24/2013.
6. US FDA CDER. Sitagliptin NDA 021995. Label 4/27/2015.
7. US FDA CDER. Exenatide NDA 021773. Label 2/25/2015.
8. US FDA CDER. Liraglutide NDA 022341. Label 3/09/2015.
9. US FDA CDER. Exenatide extended release NDA 022200. Label 3/09/2015.
10. US FDA CDER. Albiglutide BLA 125431. Label 5/07/2015.
11. US FDA CDER. Dulaglutide BLA 125469. Label 9/18/2014.
12. US FDA CDER. Canagliflozin NDA 204042. Label 5/15/2014.
13. US FDA CDER. Dapagliflozin NDA 202293. Label 8/08/2014.
14. US FDA CDER. Empagliflozin NDA 204629. Label 8/01/2014.