



Pharmacy Pearl

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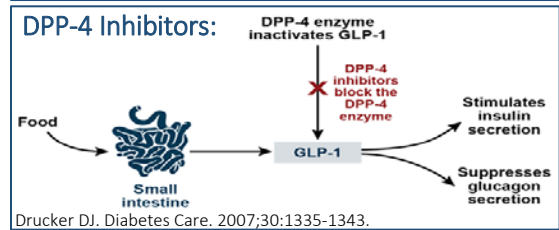
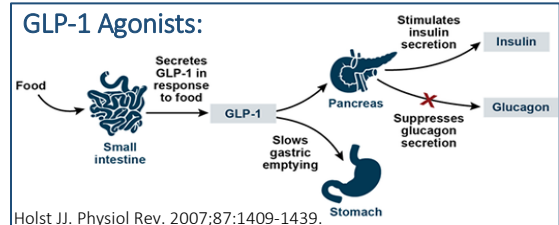
Diabetes Drugs Used in Combination (GLP-1 Agonists + DPP-4 Inhibitors) Provide No Added Benefit in T2DM

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Mechanism of Action:

Glucagon-like peptide-1 (GLP-1) receptor agonists and dipeptidyl-peptidase-4 (DPP-4) inhibitors control blood glucose by targeting the body's incretin system. GLP-1 agonists act as "incretin mimetics" and DPP-4 inhibitors prevent the breakdown of endogenous incretin.

Based on mechanism of action, it is common to think that using GLP-1 agonists and DPP-4 inhibitors in combination would result in increased incretin concentrations and improved diabetic control; however, this is not the case. Unlike endogenous incretin, GLP-1 analogues are not broken down by the DPP-4 enzyme and therefore using these medications concomitantly yields no additional benefit.



Reasons NOT to use GLP-1 agonists and DPP-4 inhibitors in combination

No additional clinical benefit	This combination was evaluated in 1 human study and demonstrated that the addition of a <i>GLP-1 agonist to patients already being treated with DPP-4 inhibitor + metformin resulted in only a 0.3% reduction in A1C</i> . This minimal decrease in A1C is much lower than the average decrease (0.8 – 2.0%) when GLP-1 agonists are used without a co-administered DPP-4 inhibitor, and is less than what would be expected if other recommended agents were added.
Increased cost to patients	No GLP-1 agonists or DPP-4 inhibitors are available generically – therefore, patients on this combination may be paying 2 brand-copays (or other brand related out of pocket cost) each time they refill their medications.
Polypharmacy	Patients with Type 2 Diabetes are likely to have additional comorbidities requiring treatment, therefore putting them at risk for polypharmacy and its associated negative outcomes.
Not approved/recommended	Use of GLP-1 agonists and DPP-4 inhibitors in combination is not approved by the FDA nor recommended by the American Diabetes Association.
Increased risk of side effects?	GLP-1 agonists and DPP-4 inhibitors have <i>similar side effect profiles</i> and are associated with an increased risk of serious events such as pancreatitis. It is unclear whether or not these risks would be additive in patients treated with these drugs in combination.

What to do if your patient is on a DPP-4 and GLP-1?

Preferred Option[#]

Continue GLP-1 agonist and Discontinue DPP-4 inhibitor

OR

Alternative Option

Continue DPP-4 inhibitor and Discontinue GLP-1 agonist

** A taper is not needed when discontinuing either medication **

[#]GLP-1 agonists result in more potent A1C reduction, are associated with weight loss (DPP-4 inhibitors are weight-neutral), and have been proven to decrease risk of negative cardiovascular outcomes (liraglutide and semaglutide), therefore superior to DPP-4 inhibitors for the treatment of Type 2 Diabetes.

Medications & Dosing Schedules:

GLP-1 Agonists

- Liraglutide (Victoza[®])
 - Lixisenatide (Adlyxin[®])
 - Exenatide (Byetta[®]) – Twice daily
 - Dulaglutide (Trulicity[®])
 - Semaglutide (Ozempic[®])
 - Exenatide ER (Bydureon[®])
- Once daily (Liraglutide, Lixisenatide)
 – Once weekly (Semaglutide, Exenatide ER)

DPP-4 Inhibitors

- Sitagliptin (Januvia[®])
 - Linagliptin (Tadjenta[®])
 - Saxagliptin (Onglyza[®])
 - Alogliptin (Nesina[®])
- Once daily