

# Diabetes Management: Avoiding Combination Therapy of GLP-1 Receptor Agonists and DPP-4 Inhibitors

## Diabetes Optimization

**Combination therapy of GLP-1 receptor agonists and DPP-4 inhibitors has no additive effect on glycemic control and increases potential side effects and cost burden to patients. Treatment with DPP-4 inhibitors should not be utilized in combination with GLP-1 receptor agonists.<sup>1,2</sup>**

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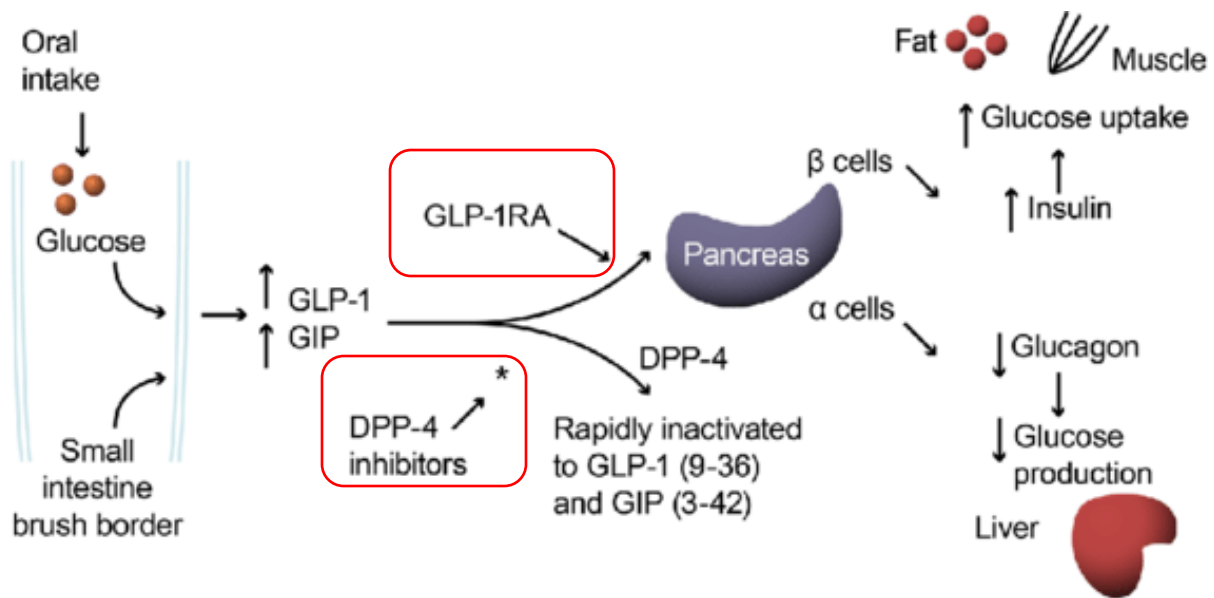
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## CLINICAL RATIONALE: WHY GUIDELINES DO NOT SUPPORT COMBINATION THERAPY

- American Diabetes Association recommends discontinuing DPP-4 inhibitors when GLP-1 agonists are initiated.<sup>3</sup>
- There are no additional glucose-lowering effects seen with combination therapy.<sup>2</sup>
- Combination of GLP-1 receptor agonists and DPP-4 inhibitors increases patient financial burden.<sup>4</sup>
- Combination therapy increases pill burden as well as the risk of side effects (gastrointestinal disturbance, pancreatitis, etc.).<sup>5</sup>

## MECHANISM OF ACTION OF GLP-1 RECEPTOR AGONIST AND DPP-4 INHIBITOR<sup>6, 7</sup>



- In response to the presence of nutrients in the small intestines, incretin hormone GLP-1 and GIP are released.
- These hormones stimulate insulin and suppress glucagon. In patients with Type 2 Diabetes, an impaired response to GLP-1 and GIP contributes to elevated blood glucose.
- DPP-4 inhibitors block the breakdown of endogenous GLP-1 and GIP, to increase levels of active hormones.
- However, GLP-1 Receptor Agonists are *designed* to resist the activity of DPP-4 inhibitors, thus combination therapy yields no benefit.

## COMPARISON OF GLP-1 RECEPTOR AGONISTS AND DPP-4 INHIBITORS

	GLP-1 Receptor Agonists	DPP-4 Inhibitors
Place in Therapy	<p><b>First line therapy</b> for patients with ASCVD or high risk for ASCVD</p> <p><b>First line therapy</b> for patients with CKD when SGLT-2 is not tolerated, or further glucose control is needed</p>	<p>Patients with contraindication to SGLT-2 and GLP-1</p> <p>Previous trial and failure of SGLT-2 and GLP-1</p> <p>Patients with no ASCVD heart failure, CKD or risk for ASCVD</p>
Formulations	Injectable (once daily or weekly option) Oral	Oral
Impact on Renal Outcomes	<b>Benefit in CKD:</b> dulaglutide, liraglutide, semaglutide (SQ)	No benefit
Impact on Cardiovascular Outcomes	<b>Benefit in ASCVD:</b> dulaglutide, liraglutide, semaglutide (SQ)	Associated with <b>increased risk of heart failure</b> (saxagliptin and alogliptin)
Weight Loss Potential	Weight loss (intermediate to high)	Weight neutral
Blood Sugar Lowering Efficacy	High to very high	Intermediate
Cost	\$\$\$	\$\$\$

## GLP-1 RECEPTOR AGONISTS AND DPP-4 INHIBITORS MEDICATIONS BY CLASS

GLP- 1 Receptor Agonists	DPP- 4 Inhibitors
<p><b>Injectable</b></p> <ul style="list-style-type: none"> <li>• Tirzapatide (<b>Mounjaro®</b>)</li> <li>• Liraglutide (<b>Victoza®</b>)</li> <li>• Lixisenatide (<b>Adlyxin®</b>)</li> <li>• Dulaglutide (<b>Trulicity®</b>)</li> <li>• Semaglutide (<b>Ozempic®</b>)</li> <li>• Combination Medications Containing GLP-1 Agonists <ul style="list-style-type: none"> <li>○ Liraglutide + Insulin Degludec (<b>Xultophy®</b>)</li> <li>○ Lixisenatide + Insulin Glargine (<b>Soliqua®</b>)</li> </ul> </li> </ul> <p><b>Oral</b></p> <ul style="list-style-type: none"> <li>• Semaglutide (<b>Rybelsus®</b>)</li> </ul>	<p><b>Oral</b></p> <ul style="list-style-type: none"> <li>• Sitagliptin (<b>Januvia®</b>)</li> <li>• Linagliptin (<b>Tradjenta®</b>)</li> <li>• Saxagliptin (<b>Onglyza®</b>)</li> <li>• Alogliptin (<b>Nesina®</b>)</li> <li>• Combination Medications Containing DPP-4 Inhibitors* <ul style="list-style-type: none"> <li>○ Alogliptin + Metformin (<b>Kazano®</b>)</li> <li>○ Alogliptin + Pioglitazone (<b>Osemi®</b>)</li> <li>○ Linagliptin + Metformin (<b>Jentadueto®</b>, <b>Jentadueto XR®</b>)</li> <li>○ Linagliptin + Empagliflozin (<b>Glyxambi®</b>)</li> <li>○ Saxagliptin + Metformin (<b>Kombiglyze XR®</b>)</li> <li>○ Saxagliptin + Dapagliflozin (<b>Qtern®</b>)</li> <li>○ Saxagliptin + Metformin + Dapagliflozin (<b>Qternet XR®</b>)</li> <li>○ Sitagliptin + Metformin (<b>Janumet®</b>, <b>Janumet XR®</b>)</li> </ul> </li> </ul> <p>*When patients discontinued combination therapy containing DPP-4 inhibitors, the other components from combination therapy should be evaluated and maintained if clinically appropriated.</p>

## REFERENCES

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