Deprescribing: Reducing Therapeutic Duplications of Incretin-Based Medications in Primary Care

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Learning Objectives

1. Explain why dipeptidyl peptidase-4 inhibitors (DPP-4i) and glucagon-like peptide-1 agonist (GLP-1a) medications do not have additive glucose reduction effects.
2. Describe the pharmacist's role in deprescribing efforts.

Introduction

- The American Diabetes Association *Standards of Care in Diabetes* (ADA Guidelines), recommends using multiple therapies for diabetes if needed to achieve glucose goals.[1]
- Duplicate therapy alerts may be missed due to alert fatigue. This is difficult when multiple medications are used to treat the same condition, for example, diabetes. According to one collaborative, drug-duplicate therapy medication events were the most commonly reported alert events. In this report, alerts were most frequently not acknowledged or bypassed.[2] It is important to balance the value of alerts with the disruption in workflow so that alerts have a positive impact on patient care.
- Polypharmacy raises the risk of unnecessary duplicate therapies which contribute to increased drug spend. This affects provider payment when participating in value-based contracts and may increase patient out-of-pocket costs.

Problem

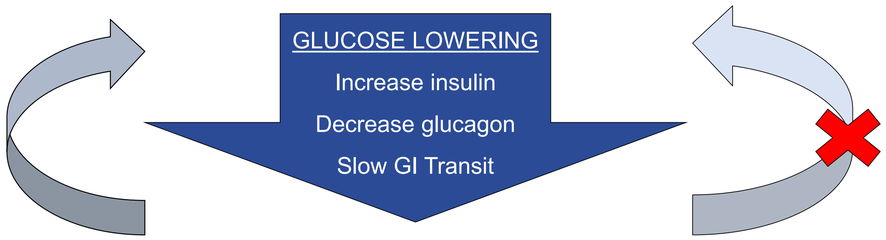
- Concurrent use of DPP-4i and GLP-1a medications has no additive effect on lowering blood glucose. Duplicate therapy alerts are often overridden; this additional drug therapy is costly and ineffective.
- Unnecessary medications may cause additional side effects without additional benefits.

Taking Both Medications Is Not Additive

GLP-1 is released by the gut in response to food

OR

GLP-1 agonist medication administered



Endogenous GLP-1 is broken down by DPP-4 enzyme and excreted.
Inhibiting DPP-4 leads to an increase in GLP-1 hormone and additional glucose lowering.

DPP-4 has no effect on GLP-1 agonist medications and the combination of DPP-4 inhibitor and GLP-1 agonist provides no additional glucose effects over GLP-1 agonist alone.

Intervention

- The initiative focused on therapeutic duplication alert overrides for GLP-1a and DPP-4i medications. A report was created to track these overrides.
- The report was reviewed weekly by a pharmacist. Patients with active DPP-4i and GLP-1a prescriptions qualify for pharmacist to provider outreach.
- Standard text was used to communicate and educate providers. Medication profiles were reviewed by the pharmacist and individualized recommendations for diabetes optimization were added.

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No one in a position to control the content of this educational activity has relevant financial relationships with ineligible companies

Results

- Usually recommend discontinuing the DPP-4i medication because it does not have the cardiovascular and weight benefits of GLP-1a.
- Between 2020-2022, 137 provider messages were sent with an 88% acceptance rate.
- In addition to avoiding ineffective duplicate therapy and often saving patient copay costs, this represents $945,000 health plan dollars saved*.

*Cost savings based on average wholesale price for 12 months of DPP-4i medication

Year	Change Accepted	Change Declined
2020	42	6
2021	35	7
2022	43	4
Total	**120**	**17**

Lessons Learned

- Duplication alerts can be missed, especially when multiple medications are required to treat a disease.
- Multifaceted approach of education and pharmacist targeted follow-up works best.
- $0 Copay cost was a factor when change was declined.

Key Takeaways

- Unnecessary medication duplications can add cost as well as amplify side effects from medications.
- Be alert for opportunities to reduce unnecessary medications.

References

[1] Diabetes Care December 2022, Vol.46, S1-S4
[2] White Paper: Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization, accessed 7/20/2023 https://d84vr99712pyz.cloudfront.net/p/pdf/hit-partnership/partnership_whitepaper_alertfatigue_final.pdf

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Target Medications

GLP-1 Agonists
Dulaglutide
Exenatide
Liraglutide
Lixisendatide
Semaglutide (SubQ or Oral)
Tirzepatide (GLP-1a/GIPa)

DPP-4 Inhibitors
Alogiptin
Linagliptin
Saxagliptin
Sitagliptin

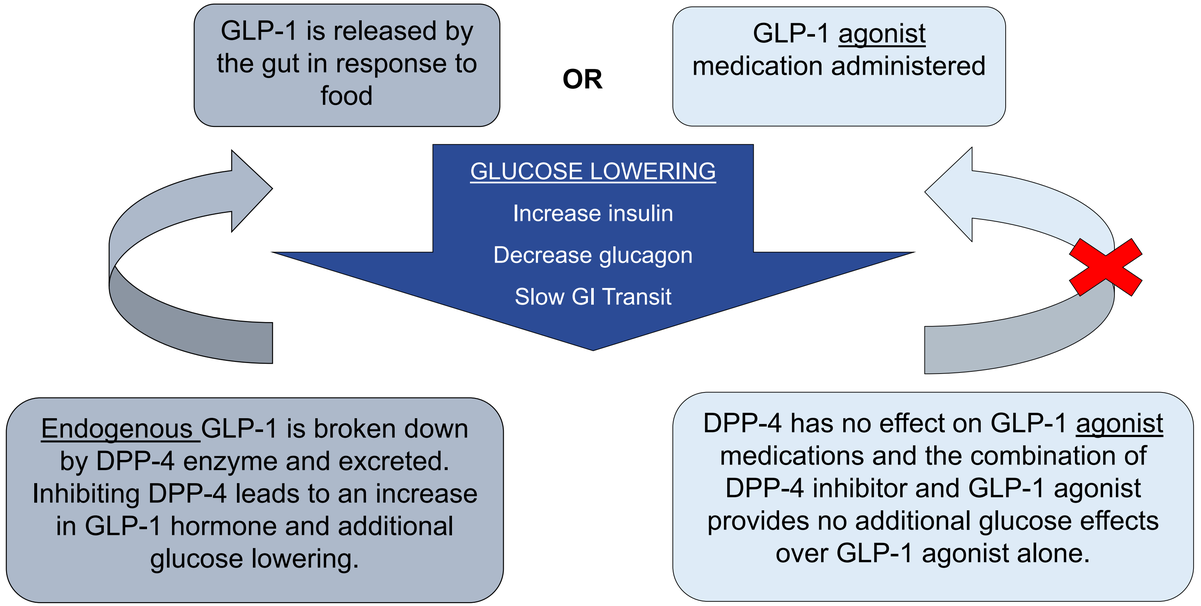
GLP-1 – Incretin hormone secreted in intestine.

- Functions to increase body's insulin release and decrease glucagon.
- GLP-1 agonists work by mimicking GLP-1; therefore, will stimulate insulin release and decrease glucagon release. GLP-1 agonists medications also slow GI transit.

DPP-4 –Functions to inactivate GLP-1 hormone prior to excretion.

- By blocking DPP-4 function, there is an increase in endogenous GLP-1 levels.
- This rise in GLP-1 stimulates endogenous insulin production and decreases glucagon.

Because GLP-1 Agonists are structurally different from natural occurring GLP-1 hormone, GLP-1 agonists drugs are not inactivated by DPP-4.



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Standard Provider Communication Template

I was performing a quality review of patients who may potentially have therapeutic duplication of incretin-based medications and noticed that your patient is prescribed both _▼ [DPP4i] and _▼[GLP1 agonist]

The combination of these 2 medications provides minimal clinical benefit. One study showed that adding GLP-1 to standard therapy (DPP4i + metformin) resulted in only an additional 0.3% reduction in A1C[3]. These medications are brand only and high-cost to patients. The combination can also cause additive side effects. Concurrent use of GLP1 agonists and DPP4 inhibitors is not included in the ADA guidelines for diabetes management.

If discontinuation of one agent is desired, it is preferred to discontinue the DPP-4. Continuation of the GLP-1 Agonist can provide cardiovascular and weight-loss benefits which are usually desired in patients with Type 2 Diabetes.

Please consider discontinuing _▼ in this patient. (It is not necessary to taper off the DPP-4 medication.)

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[3] Violante R, Oliveira JH, Yoon KH, Reed VA, Yu MB, Bachmann OP, Lüdemann J, Chan JY. A randomized non-inferiority study comparing the addition of exenatide twice daily to sitagliptin or switching from sitagliptin to exenatide twice daily in patients with type 2 diabetes experiencing inadequate glycaemic control on metformin and sitagliptin. Diabet Med. 2012 Nov;29(11):e417-24. doi: 10.1111/j.1464-5491.2012.03624.x. PMID: 22375612.