Clinical Resource Guide: DPP-4 Inhibitors (Sitagliptan, saxagliptan, linagliptin, alogliptan)

INTRODUCTION TO DPP-4 INHIBITORS

Dipeptidyl peptidase-4 (DPP-4) inhibitors are a class of oral antidiabetic medications commonly used in the management of type 2 diabetes mellitus. They work by inhibiting the enzyme DPP-4, which in turn increases the levels of active incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These hormones stimulate insulin secretion and suppress glucagon release, leading to improved glycemic control. Currently, there are several DPP-4 inhibitors available in the United States, each with its own unique characteristics and dosing considerations.

Pharmacist Corner Objectives

1.) Describe the clinical significance and mechanism of action of DPP-4 Inhibitors.
2.) Evaluate the risks involved with continuing DPP-4 Inhibitors in palliative care and end of life patients.
3.) Understand the rationale for deprescribing DPP-4 Inhibitors.

OVERVIEW AND MECHANISM OF ACTION

DPP-4 inhibitors are a class of oral antidiabetic medications that exert their therapeutic effects through the inhibition of dipeptidyl peptidase-4, an enzyme responsible for the degradation of incretin hormones. Incretins, such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), play crucial roles in regulating glucose homeostasis by stimulating insulin secretion and inhibiting glucagon release in a glucose-dependent manner.

Upon food ingestion, incretin hormones are released from the gut into the bloodstream, where they exert their effects on pancreatic β-cells and α-cells. GLP-1 stimulates insulin secretion in response to elevated blood glucose levels while simultaneously suppressing glucagon secretion, thereby reducing hepatic glucose output. Additionally, GLP-1 delays gastric emptying and promotes satiety, contributing to postprandial glucose control and weight management.

DPP-4 inhibitors, including sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina), prolong the action of endogenous incretin hormones by inhibiting their degradation. By preventing the enzymatic breakdown of GLP-1 and GIP, DPP-4 inhibitors enhance their glucose-lowering effects, leading to improved glycemic control in patients with type 2 diabetes mellitus.

It is important to note that while DPP-4 inhibitors offer a mechanism for glucose regulation that does not rely on insulin secretion, their efficacy may be limited in patients with reduced oral intake and activity, such as those in hospice or end-of-life care settings. In such cases, the decision to continue or discontinue DPP-4 inhibitors should be guided by individual patient factors, goals of care, and the overall management approach in the hospice setting

Generic Name	Trade Name	Daily Dose	Monthly Cost
Sitagliptin	Januvia	100mg	$300-$400
Saxagliptin	Onglyza	2.5-5mg	$300-$400
Linagliptin	Tradjenta	5mg	$300-$400
Alogliptin	Nesina	25mg	$300-$400

The benefits seen with SGLT2 Inhibitors are typically not applicable to the goals of the hospice patient as they provide no symptom management or relief.

CLINICAL CONSIDERATIONS IN HOSPICE

In hospice care, the management of diabetes differs from traditional approaches, focusing on alleviating symptoms and improving quality of life rather than achieving strict glycemic control. Therefore, the use of DPP-4 inhibitors in hospice patients should be carefully evaluated. Discontinuation of DPP-4 inhibitors may be warranted in patients with limited life expectancy, as these medications may add unnecessary complexity to medication regimens without significant benefits in end-of-life care. However, individual patient factors, such as comorbidities and preferences, should always be considered when making clinical decisions.

RATIONALE FOR DISCONTINUING DPP-4 INHIBITORS IN THE HOSPICE SETTING

Discontinuing DPP-4 inhibitors in hospice patients is often warranted due to various considerations, including their potential side effects and limited efficacy in end-of-life care. Table 2 outlines the common side effects associated with DPP-4 inhibitors and highlights their lack of efficacy in patients with limited oral intake and activity, such as those in the end-of-life setting.

In addition to potential side effects, DPP-4 inhibitors may have limited efficacy in hospice patients due to factors such as reduced oral intake and decreased physical activity commonly observed in end-of-life care. These medications primarily target glucose control through incretin hormone modulation, which may not provide significant benefits in patients with limited life expectancy or in those experiencing terminal decline. Therefore, discontinuing DPP-

4 inhibitors can help streamline medication regimens, reduce pill burden, and optimize comfort for hospice patients nearing the end of life.

SIDE EFFECT	DESCRIPTION
Hypoglycemia	Risk of hypoglycemia may be increased, especially when combined with other antidiabetic agents.
Upper Respiratory Tract Infections	Nasopharyngitis, sinusitis, and upper respiratory tract infections are among the most common adverse effects reported.
Gastrointestinal Symptoms	Nausea, diarrhea, and abdominal discomfort may occur, although less frequently.
Headache	Headache is a relatively common side effect reported with DPP-4 inhibitors.
Joint Pain	Arthralgia and musculoskeletal pain have been reported, albeit infrequently.
Pancreatitis	Rare cases of acute pancreatitis have been reported with DPP-4 inhibitor use.

ALTERNATIVES TO DPP-4 INHIBITORS IN THE HOSPICE SETTING

In lieu of DPP-4 inhibitors, alternative strategies for managing diabetes in hospice patients may include the judicious use of insulin therapy. Subcutaneous insulin can be titrated to prevent symptomatic hyperglycemia while providing flexibility in dosing and administration. Short-acting insulin formulations, such as regular insulin or rapid-acting insulin analogs, are preferred for their rapid onset of action and shorter duration of effect. However, the decision to initiate insulin therapy should be individualized based on the patient's clinical status, preferences, and goals of care.

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