Best Practice Message

September 2021

Focus on Diabetes: Dulaglutide and empagliflozin treatment decision

Practice changing moments

- Consider a GLP-1 or SGLT-2 as beneficial cardiovascular and renal medicines in patients with Diabetes.
- Patients cannot receive funded treatment of dulaglutide and empagliflozin together. The decision between which agent to select is patient specific and must be individualised.
- Vildagliptin should be stopped prior to starting dulaglutide.
- Full treatment decision algorithms for empagliflozin and dulaglutide (including talking points with patients and prescribing advice) are available from akohiringa.co.nz

Introduction

Dulaglutide, a Glucagon-Like peptide-1 receptor agonist (GLP-1 RA) is funded from the 1st of September. GLP-1 RAs stimulate the glucose dependent insulin release from the pancreas, also slowing gastric emptying and inhibiting post-meal glucagon release.[1] This causes reductions in glucose levels and weight loss. Due to its long half-life dulaglutide will have a more pronounced effect on fasting glucose levels than postprandial glucose.[2]

Empagliflozin has been funded since 1st of February. Empagliflozin is a Sodium glucose transport protein 2 (SGLT-2) inhibitor. SGLT-2 inhibitors prevent the reabsorption of glucose in the proximal convoluted tubule causing increased excretion of glucose into the urine. Both classes of medication have proven cardiovascular and renal benefits in patients with type 2 diabetes.[3–6]

Choosing between empagliflozin and dulaglutide

Patients with diabetic renal disease, heart failure, known cardiovascular disease or 5 year risk of CVD greater than 15% should be offered to initiate dulaglutide or empagliflozin as a second line medication (after metformin) provided they meet the relevant special authority criteria (see appendix below).

	Dulaglutide	Empagliflozin
Favouring selection	• History of primarily atherosclerotic -disease • Patient is obese • Preference for once weekly injection over daily oral therapy • Empagliflozin is contraindicated or not tolerated due to adverse effects	• History of heart failure • History of diabetic kidney disease with albuminuria (eGFR >30mL/min/1.73m^2) • Preference for oral therapy over injection • Dulaglutide is contraindicated or not tolerated due to adverse effects
Use with caution/avoid use	• eGFR <15mL/min/1.73m^2 • History of severe gastrointestinal disorders or gastric surgery • History of Pancreatitis • Frail elderly or others where weight loss is undesirable	• eGFR <30mL/min/1.73m^2 • History of severe genitourinary infection • Frail elderly or others where weight loss is undesirable or those at risk of volume depletion • Patients wanting to try keto diets • History of diabetic ketoacidosis • High alcohol intake

NZSSD and international guidelines recommend a combination of a GLP-1 RA and SGLT-2 inhibitor to achieve glycaemic targets and reduce cardiovascular and renal complications of diabetes. Discuss with patients the option of self funding empagliflozin.

Who should not be started on dulaglutide?

There is currently not enough data to support the use of dulaglutide or other GLP-1 RAs in patients under the age of 18 or in the management of patients who are pregnant or breastfeeding.[7,8] Due to the risk of exacerbating current symptoms, dulaglutide should not be used in patients who have severe gastrointestinal disease including gastroparesis. Dulaglutide should also be avoided in patients with a history of pancreatitis, Medullary thyroid carcinoma or MEN2 syndrome.[7,8] Note that patients who are currently taking vildagliptin must have this stopped prior to initiating treatment with dulaglutide. There is no synergistic benefit in combining DPPIV inhibitor therapy with GLP-1 RA therapy.[9]

Who should not be started on empagliflozin?

There is currently not enough data to support the use of empagliflozin or other SGLT-2 inhibitors in patients under the age of 18 or in the management of patients who are pregnant or breastfeeding.[7,8] Because of the increased urinary excretion of glucose, patients have an increased risk of genitourinary infections and increased diuresis. Patients with previous severe genitourinary infections should not be initiated on empagliflozin. While empagliflozin can slow the progression of diabetic kidney disease, it is contraindicated in patients with an eGFR <30mL/min/1.73m^2. Canagliflozin, another SGLT-2 inhibitor was found to increase the risk of bone fractures[10]. There is currently insufficient evidence to determine if this is a class effect however, caution is advised in patients who have osteoporosis or are a high falls risk.

Other resources:

- New Zealand society for the study of diabetes management algorithm: https://t2dm.nzssd.org.nz/Management-Algorithm.html
- He Ako Hiringa have treatment initiation algorithms for both dulaglutide and empagliflozin: https://www.akohiringa.co.nz/tags/diabetes
- Health navigator patient resources: https://www.healthnavigator.org.nz/medicines/d/dulaglutide/
- NZF: dulaglutide - New Zealand Formulary (nzf.org.nz)

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Appendix 1:

Special authority criteria for Dulaglutide and empagliflozin[11,12]:

☐ Patient has previously received an initial approval for an SGLT2 inhibitor/GLP-1 agonist

OR

☐ Patient has type 2 diabetes

AND

At least ONE of the following:

- ☐ Patient is Māori or any pacific ethnicity
- ☐ Patient has pre-existing cardiovascular disease or risk equivalent
- ☐ Patient has an absolute 5-year cardiovascular disease risk of 15% or greater according to a validated cardiovascular risk assessment calculator
- ☐ Patient has a high lifetime cardiovascular risk due to being diagnosed with type 2 diabetes during childhood or as a young adult
- ☐ Patient has diabetic kidney disease

AND

☐ Target HbA1c (of 53 mmol/mol or less) has not been achieved despite the regular use of at least one blood-glucose lowering agent (e.g. metformin, vildagliptin, or insulin) for at least 3 months

Note: Not to be given in combination with each other

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