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**Joint Position Statement Regarding the Concurrent Use of Sodium Glucose Co-transporter 2 Inhibitors and Glucagon Like Peptide-1 Receptor Agonists in Patients with Type 2 Diabetes**

This position statement is produced by the Hong Kong Society of Endocrinology, Metabolism and Reproduction (HKSEMR), Diabetes Hongkong (DHK), Diabetologists and Endocrinologists Alliance (DEA), and the contents are supported by the Division of Endocrinology and Diabetes, Department of Medicine and Therapeutics of the Chinese University of Hong Kong (CUHK), the Division of Endocrinology and Metabolism, Department of Medicine, School of Clinical Medicine of the University of Hong Kong (HKU), and the Hong Kong College of Physicians (HKCP). It is issued in response to the concerns reported recently in the media about the concurrent use of sodium glucose co-transporter 2 inhibitors (SGLT2i) and glucagon like peptide-1 receptor agonists (GLP1rA), a combination which is not uncommonly prescribed in patients with type 2 diabetes. The objective of this statement is to reassure the public that **the concurrent use of SGLT2i and GLP1rA, when clinically indicated, is well supported by current professional guidelines for clinical management of type 2 diabetes**, and the **efficacy of this combination has been substantiated with ample scientific evidence**.

Both SGLT2i and GLP1rA are anti-diabetic agents with beneficial effects on glycaemic control and cardiovascular risk factors, which include body weight, blood pressure and lipid profile, and with minimal risk of hypoglycaemia. Moreover, SGLT2i and some GLP1rA possess cardio- and reno-protective effects as demonstrated in several multi-centre randomized controlled studies over the past few years. (1) Therefore, the concurrent use of SGLT2i and GLP1rA has been recommended for glycaemic control by the American Diabetes Association since 2017. (1) (2) Indeed, the concurrent use of SGLT2i and GLP1rA in patients with type 2 diabetes and atherosclerotic cardiovascular disease, heart failure, chronic kidney disease, or those with a compelling need to minimize hypoglycaemia or weight gain, has further been reinforced in the Standards of Medical Care in Diabetes by the American Diabetes Association since 2019. (1) (3) (4) (5)

The superior efficacy in glycaemic control and cardiovascular risk factors with this combination over the addition of either SGLT2i or GLP1rA to background anti-diabetic therapy has been demonstrated in several large-scale randomized controlled trials such as DURATION-8 (exenatide weekly plus dapagliflozin), AWARD-10 (dulaglutide plus dapagliflozin or empagliflozin) and SUSTAIN-9 (semaglutide plus canagliflozin or dapagliflozin or empagliflozin). (6-8) Notably, SGLT2i and GLP1rA were simultaneously initiated in DURATION-8 and none of the participants on this combination therapy had diabetic ketoacidosis. (6)

Taken together, the current evidence demonstrates that the concurrent use of SGLT2i and GLP1rA is both efficacious and safe. Nevertheless, due caution is required when both SGLT2i and GLP1rA are initiated simultaneously. Patients with diabetes can have complex phenotypes, and insulin insufficiency can be present despite being overweight. In patients with or at risk of insulin insufficiency, as might occur in patients with long duration of disease, when there are multiple complications, or high HbA1c despite adhering to treatment with multiple medications, (especially when accompanied by weight loss and low C-peptide level), SGLT2i should always be used with caution. Insulin enables effective use of glucose as a normal fuel substrate and prevents lipolysis as an alternative fuel. Therefore, patients who are at risk of insulin insufficiency should be considered for treatment with insulin first to prevent lipolysis that can precipitate ketosis, especially during acute stressful events such as infections, surgery, or prolonged fasting. At all times, we recommend clinicians to alert patients the need of sick day management before initiating SGLT2i, and to remind patients to withhold SGLT2i during acute illness and to seek medical attention if they experience symptoms of ketoacidosis. Patients should be counselled to understand that ketoacidosis, though uncommon, is a serious potential adverse event of SGLT2i.

**References**

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