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Sodium-glucose co-transporter 2 (SGLT2) inhibitors in cardiac and renal disease

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- Initially licensed for the management of type 2 diabetes (T2DM), large placebo-controlled trials have shown cardiovascular and renal benefits of sodium-glucose co-transporter 2 (SGLT2) inhibitors.
- In addition to their indication in the management of T2DM, the SGLT2 inhibitors dapagliflozin and empagliflozin are also licensed for the treatment of heart failure and chronic kidney disease.
- SGLT2 inhibitors have been shown to be safe, with urinary tract and fungal genital infections among the most commonly reported adverse effects.
- More serious, but less common adverse effects highly unlikely to affect people without diabetes include ketoacidosis, lower limb amputation and Fournier's gangrene.
- 'Sick day guidance' should be provided to all those on SGLT2 inhibitor therapy, including advice that SGLT2 inhibitors should be held if acutely unwell, especially if at risk of dehydration.

Introduction

Sodium-glucose co-transporter 2 (SGLT2) inhibitors (sometimes referred to as 'gliflozins' or 'flozins') first became available in the EU with the authorisation of dapagliflozin by the European Medicines Agency in 2012 for the treatment of type 2 diabetes (T2DM)[1] (approved for reimbursement in Ireland in 2015[2]). Further SGLT2 inhibitors (i.e., canagliflozin, empagliflozin and ertugliflozin) were subsequently licensed and launched in Ireland for T2DM.[3-5] Large placebo-controlled trials have since demonstrated benefits of SGLT2 inhibitors for cardiovascular disease (CVD) and renal outcomes, regardless of diabetic status[6,7], with dapagliflozin and empagliflozin now licensed for the treatment of both symptomatic chronic heart failure (HF) and chronic kidney disease (CKD)[1,4]. While there is less evidence currently to demonstrate the cardiovascular benefits of ertugliflozin than there is for dapagliflozin, empagliflozin and canagliflozin[8], it has been suggested that the beneficial effects of SGLT2 inhibition on risk of heart failure hospitalisation and kidney disease progression are likely to be a class effect[6].

With SGLT2 inhibitors now included in clinical guidelines for the **management of HF**[9,10] **and CKD**[6,11], this bulletin aims to provide an overview of the key considerations needed to ensure their safe and effective use in adults, with a focus on these conditions.

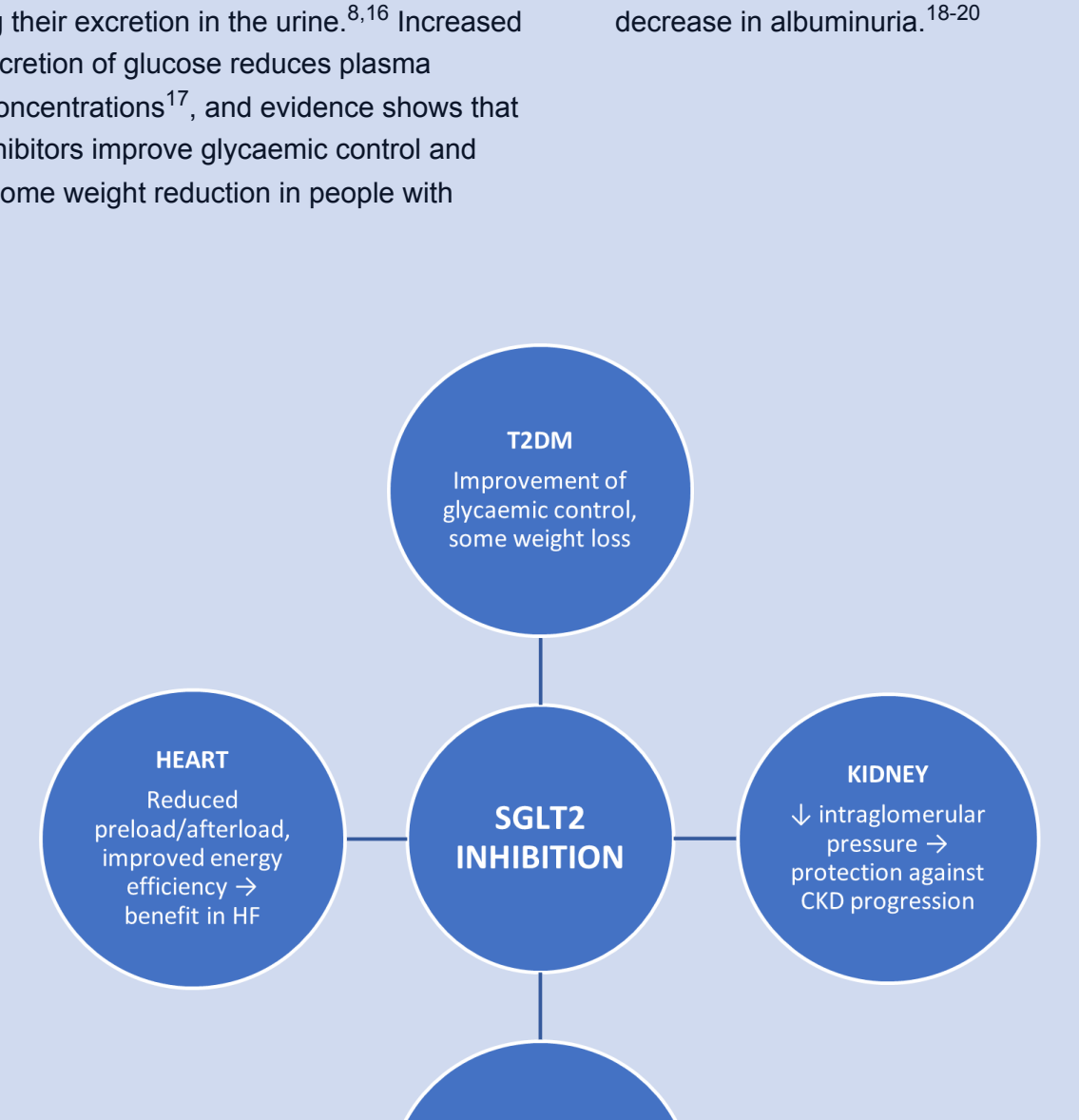
SGLT2 inhibitors in Ireland: licensing and utilisation

The SGLT2 inhibitors dapagliflozin, empagliflozin, canagliflozin, and ertugliflozin are licensed for the treatment of T2DM[1,3-5]; dapagliflozin and empagliflozin have additional indications for the treatment of HF and CKD[1,4]. HSE Primary Care Reimbursement Schemes (PCRS) data indicate that the number of people in receipt of SGLT2 inhibitors in Ireland rose from approximately 28,000 in 2019 to over 97,000 by the end of 2025.[12]

How do SGLT2 inhibitors work?

Glucose is normally filtered in the kidneys and is reabsorbed in the proximal tubules, with the majority reabsorbed via the very high-capacity glucose transporter SGLT2, through an active process that also involves the reabsorption of sodium.[13-15] By reversibly inhibiting the glucose transporter SGLT2, the SGLT2 inhibitors reduce the reabsorption of glucose and sodium into the blood, increasing their excretion in the urine.[8,16] Increased urinary excretion of glucose reduces plasma glucose concentrations[17], and evidence shows that SGLT2 inhibitors improve glycaemic control and promote some weight reduction in people with T2DM[16].

Sodium reabsorption is also reduced, with the resulting natriuresis decreasing intravascular volume and blood pressure, leading to a reduction in cardiac preload and afterload.[13] The increased distal sodium delivery and inhibition of tubuloglomerular feedback results in afferent vasoconstriction and a reduction in intraglomerular pressure, which leads to a decrease in albuminuria.[18-20]



Place in therapy

Since February 2026, the UK National Institute for Health and Care Excellence (NICE) has recommended an SGLT2 inhibitor in combination with metformin as the standard initial treatment for people with **T2DM and no relevant comorbidity**.[21]

The benefits of SGLT2 inhibitors, demonstrated in recent trials* evaluating cardiac and renal outcomes, are now also reflected in **guideline recommendations** for the use of SGLT2 inhibitors in **cardiac and renal disease**, a selection of which, for the purposes of this bulletin, are highlighted in the sections to follow.

Cardiovascular disease guidance

Heart failure

SGLT2 inhibitors are one of the 'four pillars' of medicine classes forming the cornerstone of heart failure with **reduced** ejection fraction (HFrEF) management[22], alongside an angiotensin-converting enzyme (ACE) inhibitor (or angiotensin receptor-neprilysin inhibitor (ARNI) or angiotensin II receptor blocker (ARB)), a beta-blocker and a mineralocorticoid receptor antagonist[10].

The SGLT2 inhibitors dapagliflozin and empagliflozin are now also currently recommended by UK National Institute for Health and Care Excellence (NICE) for patients with symptomatic HF and preserved (HFpEF) or mildly reduced ejection fraction (HFmrEF)[10], and the European Society of Cardiology (ESC) have recently recommended SGLT2 inhibitors for all symptomatic patients with HF, **regardless of left ventricular ejection fraction**[9].

T2DM and atherosclerotic CVD (ASCVD)

SGLT2 inhibitors are further recommended by the ESC in patients with T2DM and atherosclerotic CVD (ASCVD) to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.[23]

Chronic kidney disease (CKD) guidance

In the UK, dapagliflozin or empagliflozin are recommended by **NICE**[11,24,25] as options to treat CKD as an add-on to optimised standard care in adults with either:

(i) an estimated glomerular filtration rate (eGFR) of between 20 mL/min/1.73 m^2 and < 45 mL/min/1.73 m^2, or
(ii) an eGFR between 45 mL/min/1.73 m^2 and 90 mL/min/1.73 m^2, and either a urine albumin-to-creatinine ratio (uACR) of ≥ 22.6 mg/mmol or T2DM.[11,24,25]

The **UK Kidney Association (UKKA)** provides guidance on the use of SGLT2 inhibitors in those with CKD[26] (irrespective of primary kidney disease*), recommending their initiation in specific populations including:

People with T2DM, for any of the four clinical scenarios:

(i) eGFR of 20–45 mL/min/1.73 m^2, or
(ii) eGFR > 45 mL/min/1.73 m^2 and a uACR of ≥ 25 mg/mmol, or
(iii) Symptomatic HF, irrespective of ejection fraction, or
(iv) Established coronary disease.[26]

People without T2DM, with:

(i) eGFR of ≥ 20 mL/min/1.73m^2 and a uACR of ≥ 25 mg/mmol, or
(ii) Symptomatic HF, irrespective of ejection fraction.[26]

[*Excludes people with polycystic kidney disease, type 1 diabetes, or a kidney transplant[26].*]

Further recommendations on the use of SGLT2 inhibitors for CKD are available in the full text of this UKKA guideline.[26]

Kidney Disease: Improving Global Outcomes (KDIGO) CKD guidelines (2024)[27] recommend use of SGLT2 inhibitors in specific populations, including adults with:

(i) T2DM, CKD, and an eGFR ≥ 20 mL/min/1.73 m^2, or
(ii) CKD and eGFR ≥ 20 mL/min/1.73 m^2 with uACR ≥ 20 mg/mmol, or
(iii) CKD and HF, irrespective of level of albuminuria.[27]

Key practice points to consider when starting SGLT2 inhibitor therapy

A note on type 1 diabetes

Due to an increased risk of diabetic ketoacidosis (DKA), SGLT2 inhibitors should **not** be used for the treatment of type 1 diabetes (T1DM).[1,3-5,8,13] It is also advised that SGLT2 inhibitors should generally not be used to treat other conditions (e.g., HF, CKD) in people with T1DM, as this cohort of patients was excluded from trials.[13] The UKKA comments that there is currently insufficient evidence to recommend the use of SGLT2 inhibitors as an adjunct to existing therapies in the management of diabetic nephropathy in people with T1DM, advising that SGLT2 inhibitors should be initiated in people with T1DM only under the strict direction of the diabetes team.[6]

Cautions and adverse effects

In addition to their well-established efficacy, SGLT2 inhibitors have been shown to be safe[6] and generally well-tolerated[7,28]. Serious adverse effects of SGLT2 inhibitors are rare, particularly among people without diabetes.[6] The likelihood of experiencing an adverse drug reaction (ADR) with SGLT2 inhibitor therapy may depend on individual patient factors including e.g., **whether they have a diagnosis of diabetes**, their age and their level of frailty.[26] The most common ADRs associated with the use of SGLT2 inhibitors are discussed in the sections to follow.

Volume depletion

Due to their combined osmotic diuretic and natriuretic effect, SGLT2 inhibitors can cause or aggravate volume depletion[6,13] leading to **dehydration and hypotension**, particularly in older people[13,17] and/or those on concurrent antihypertensive medicines or diuretics[17,29]. Hypovolaemia should be corrected before SGLT2 inhibitor initiation[8,13] and those on diuretics should be advised to seek medical attention if they develop symptoms of volume depletion after starting SGLT2 inhibitor therapy[6]. Early clinical review and if appropriate, a diuretic or antihypertensive dose reduction may need to be considered in individuals deemed at high risk of hypovolaemia.[6] Temporary interruption of treatment with SGLT2 inhibitors is recommended for those who develop volume depletion until the depletion is corrected.[1,3-5] [See also 'Sick day guidance']

In the initial few weeks following the introduction of an SGLT2 inhibitor, creatinine levels may increase and a reduction in eGFR may be observed.[1,3-5,26] This reduction in eGFR is generally relatively small and largely reversible, and the major studies have not demonstrated an increased risk of acute kidney injury (AKI) in people treated with SGLT2 inhibitors.[26]

The UKKA highlight that any early changes in eGFR should not usually be considered an adverse effect of the medicines, and that it is important that it **should not routinely result in withdrawal of SGLT2 inhibitor therapy** in those who are likely to gain significant benefit from this class of medicines.[26] [See 'Monitoring parameters']

Infections

Commonly reported adverse effects of SGLT2 inhibitors include dysuria, polyuria, and genital and urinary tract infections[30]; urinary symptoms and the increase in rates of infection may be related to urinary glucose excretion[1,5,8,30,31]. Whilst acknowledging the value of SGLT2 inhibitors, the American Geriatrics Society (AGS) Beers Criteria® include SGLT2 inhibitors as medicines to be used with caution in older adults as they may be at increased risk of urogenital infections, particularly women in the first month of treatment; **active monitoring** for these possible adverse effects is advised.[32]

- Urinary tract infection (UTI)

Although randomised data from major trials show that the increased risk of UTIs with SGLT2 inhibitors is small, the UKKA acknowledges that these medicines are being prescribed in people who have a high risk of UTIs and recommends that **effective prompt management of any infection should be undertaken**.[6] Advise patients about this potential adverse effect[28] and temporarily discontinue SGLT2 inhibitors when treating acute pyelonephritis or urosepsis[1,3-6].

- Fungal genital infections and Fournier's gangrene

SGLT2 inhibitors have been associated with an increased risk of **genitourinary fungal infection**.[6,13] Self-care to maintain good genital hygiene may reduce the risk of these infections[6,7], which are usually mild and easily treated[6,17]. Healthcare professionals should ensure that people prescribed SGLT2 inhibitors are aware of this complication, how to reduce their risk and the appropriate action to take should they develop symptoms.[6] Most people can continue SGLT2 inhibitor therapy during the treatment of fungal genital infections.[6,31]

In contrast, rare but serious and potentially life-threatening cases of **Fournier's gangrene** (necrotising fasciitis of the genitalia or perineum) have been reported in people taking SGLT2 inhibitors.[6,8,13] If Fournier's gangrene is suspected, the SGLT2 inhibitor should be stopped and treatment (including antibiotics and surgical debridement) urgently started.[8] All people on SGLT2 inhibitors should be advised of the risk of Fournier's gangrene and to seek urgent medical attention if they have severe pain, tenderness, erythema or swelling in the genital or perineal area accompanied by fever or malaise.[1,3-5,8,13]

Ketoacidosis

Rare, but serious, and sometimes life-threatening and fatal cases of DKA have been reported in patients taking SGLT2 inhibitors for the treatment of T2DM[8,33]; **it is more commonly found in conjunction with dehydration or infection**[6]. In a number of the reports, the presentation of DKA was atypical, with only moderately increased blood glucose values[1,3-5,8,33] which can lead to misdiagnosis, prevent timely initiation of treatment, and negatively influence duration of illness[17]. In addition, SGLT2 inhibitor-mediated increases in urinary glucose loss may persist for several days after discontinuation which may impact duration of illness in patients who develop ketoacidosis.[17]

People with T2DM at greater risk of developing DKA include those following a very-low-carbohydrate or ketogenic diet[17,31], those with low beta cell reserve[8,31], dose decreases or missed doses of insulin[17] and alcohol abuse[8,13,17]. The UKKA recommend that people taking SGLT2 inhibitors should be advised **against** following a ketogenic diet.[6] Although DKA was observed in people who were taking an SGLT2 inhibitor for the treatment of diabetes, it is an ADR that should be considered for all people with diabetes requiring SGLT2 inhibition for treatment of CKD or heart failure.[13] To reduce DKA risk, advise people to pause their SGLT2 inhibitor if they are unwell and not able to eat and drink normally, then restart once recovered.[34] [See 'Sick day guidance']

People prescribed SGLT2 inhibitors should be educated about the signs and symptoms of DKA, (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat)[8], and advised to seek immediate medical advice if they develop any of these[6,8]. **SGLT2 inhibitor therapy should be discontinued if DKA is suspected or diagnosed**, and people with signs and symptoms of DKA should be tested for raised ketones, **even if plasma glucose levels are near-normal**.[8]

Regulatory authorities have issued recommendations to interrupt treatment with SGLT2 inhibitors in patients hospitalised for major surgical procedures or acute illness due to an increased risk of DKA (including in the presence of euglycaemia).[8,33] They have also further advised on the need for increased monitoring of **blood ketones** following interruption of SGLT2 inhibitor therapy in these people.[8,33] It should be remembered that urine measurement of ketone bodies may be less reliable compared to blood testing, as there is evidence that SGLT2 inhibitors may diminish the excretion of ketone bodies in the urine.[33] [See 'Perioperative management']

It has been suggested that after an episode of DKA and only where another clear precipitating factor has been identified, there should be discussion with the person and clinical team to establish whether the benefits of re-introducing an SGLT2 inhibitor outweigh the risks.[6]

Lower limb amputations

There are conflicting data involving the risk of lower limb amputations with SGLT2 inhibitor therapy[17,31]; canagliflozin, specifically, has been of concern[17]. Risk factors have been identified, which include prior amputation, peripheral vascular disease (PVD), neuropathy, diabetic foot ulcers, CVD, age ≥ 65 years and lack of preventative foot care, however no specific physiological mechanisms for SGLT2 inhibitor-induced amputations have been established.[17]

The UKKA suggests avoiding initiation of SGLT2 inhibitors in the presence of active foot disease (infection, ulceration and ischaemia) and withholding treatment in those who develop foot complications whilst taking an SGLT2 inhibitor.[6] It is highlighted, however, the importance of recognising people with PVD as a group of individuals who may have more to gain from the initiation of SGLT2 inhibitors with regard to protection against risk of CV death, myocardial infarction, HF complications and progression of CKD, than the associated risks of treatment.[6] People with diabetes prescribed SGLT2 inhibitors should be provided with education on routine preventative foot care.[1,31]

Fractures

Although an increased risk of fractures was reported with canagliflozin, the evidence linking SGLT2 inhibitors with changes in bone metabolism and fracture risk is uncertain.[13] It has been suggested that fracture risk might be a consequence of falls related to SGLT2 inhibitor-mediated volume depletion and hypotension, rather than a direct impact on skeletal physiology.[31,35] People with CKD are at increased risk of bone disease; monitoring of bone parameters should be performed as appropriate for CKD stage and interventions to maintain good bone health should be undertaken irrespective of the use of SGLT2 inhibitors.[6]

Frailty

Frailty describes a state of vulnerability due to advanced biological age as opposed to chronological age, and affected people are at increased risk of medication related harm.[36] The adverse effect profile of SGLT2 inhibitors needs to be considered in those living with frailty (e.g., risk of genitourinary infections, volume depletion).[37,38] However, the UKKA highlights that many of these people with frailty, and particularly those with HF, are likely to achieve significant benefit from the use of SGLT2 inhibitors.[6] When considering SGLT2 inhibitor treatment in someone with frailty, a regularly reviewed, individualised management plan, balancing disease and treatment burden is suggested, taking into account the person's health priorities and preferences, and their concomitant medication.[6,36,38]

Other considerations: dosing and use in special populations

Dosing

SGLT2 inhibitors are administered in oral formulations; the licensed doses are outlined in Table 1. Of note, some SGLT2 inhibitors are also available as combination preparations with other medicines for T2DM.

Table 1. Dosing of SGLT2 inhibitors[1,3-5] [*See later sections for dosing in hepatic/renal impairment*]

	T2DM	HF	CKD
Dapagliflozin	10 mg orally once daily	10 mg once daily	10 mg once daily
Empagliflozin	10 mg orally once daily, increased to 25 mg once daily if necessary and if tolerated in those with an eGFR ≥ 60 mL/min/1.73 m^2	10 mg once daily	10 mg once daily
Canagliflozin	100 mg orally once daily, increased if required and if tolerated to 300 mg once daily in those with an eGFR ≥ 60 mL/min/1.73 m^2	*Not licensed for this indication*	*Not licensed for this indication*
Ertugliflozin	5 mg orally once daily; can be increased to 15 mg once daily if necessary and if tolerated	*Not licensed for this indication*	*Not licensed for this indication*

eGFR = estimated glomerular filtration rate; T2DM = type 2 diabetes; HF = heart failure; CKD = chronic kidney disease. Full prescribing details are available in the Summary of Product Characteristics (SmPC) at www.hpra.ie or www.medicines.ie.

Use in special populations

Hepatic impairment

No dose adjustment of SGLT2 inhibitors is required in mild or moderate hepatic impairment.[1,3-5,20] Due to limited information, it is recommended to avoid the use of canagliflozin, empagliflozin or ertugliflozin in severe hepatic impairment.[3-5] A starting daily dose of 5 milligrams dapagliflozin can be used with caution in people with severe hepatic impairment; if well tolerated, the dose may be increased to dapagliflozin 10 milligrams once daily.[1]

Renal impairment

The efficacy of SGLT2 inhibitors for glycaemic control is dependent on renal function, meaning that they have less **glycaemic** benefit as eGFR declines.[15,17] Glycaemic efficacy is reduced in moderate renal impairment and likely absent in those with severe renal impairment; if required, consider additional glucose lowering therapy for the treatment of T2DM.[1,3-5] The individual Summary of Product Characteristics (SmPC) should be consulted for the **licensed** information on dosing in renal impairment. Of note, this may not reflect use of SGLT2 inhibitors recommended by specialists e.g., to slow progression of CKD. The UKKA guideline on SGLT2 inhibitors in kidney disease recommends that once started, SGLT2 inhibition can be continued until the need for dialysis or kidney transplantation arises (in those with and without T2DM).[6]

See 'Volume depletion' and 'Monitoring parameters' sections for information on an initial decline in renal function on starting SGLT2 inhibitors.

Older adults

There is no SGLT2 inhibitor dose adjustment recommended based on age, however elderly people may be at a greater risk of adverse effects including dehydration, genital candidiasis and UTIs.[38] [See 'Frailty']

Pregnancy and breastfeeding

There are no or limited outcome data following the use of SGLT2 inhibitors in pregnant women and therefore their use in pregnancy is not recommended.[1,3-5,8,13] Family planning is advised as part of routine diabetic care for people taking glucose-lowering medications[17,39] and standard practice has been to switch SGLT2 inhibitors to insulin in the preconception period and for the duration of pregnancy[26]. The UKKA recommend that women of child-bearing potential should be counselled prior to conception on the risks of SGLT2 inhibitors during pregnancy and they suggest that SGLT2 inhibitor therapy is discontinued upon planning, suspicion or confirmation of pregnancy.[6]

Similarly, there is no information on the clinical use of SGLT2 inhibitors during breastfeeding and therefore alternative agents may be preferred, especially while nursing a newborn or preterm infant.[6,40-43]

Other considerations: drug interactions

The metabolism of SGLT2 inhibitors is primarily via glucuronidation by UDP-glucuronosyltransferases (UGTs)[1,3-5,20]; **cytochrome P450 mediated metabolism of SGLT2 inhibitors is minimal**[20]. Examples of potential drug interactions with SGLT2 inhibitors (not exhaustive) are outlined in Table 2.

Table 2. Examples of potential drug interactions with SGLT2 inhibitors* [*not exhaustive*]

Potential interactant	Nature of drug interaction	Management
Insulin and insulin secretagogues (e.g., sulfonylureas including gliclazide)	**Hypoglycaemia**: SGLT2 inhibitors on their own do not generally cause hypoglycaemia[26], however this can occur if used **with** other diabetes medicines that carry this risk, such as insulin or medicines that stimulate insulin secretion (insulin secretagogues).[1,3-5,8,26]	Doses of concomitant insulin or insulin secretagogues may need to be decreased to reduce the risk of hypoglycaemia when initiating SGLT2 inhibitor therapy in patients with T2DM.[1,3-5,8] Factors to consider include the underlying blood glucose control of the person and their renal function.[26]
Diuretics	**Additive diuretic effect**: SGLT2 inhibitors may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and **hypotension**.[3-5,8,44]	Counsel people also taking diuretics on the symptoms of hypovolaemia and advise to seek medical attention if they develop any such symptoms after starting SGLT2 inhibitors.[6]
Antihypertensives	**Additive antihypertensive effect**: SGLT2 inhibitors can cause a modest reduction in systolic blood pressure.[15]	Caution should be exercised in patients for whom an SGLT2 inhibitor-induced drop in blood pressure could pose a risk, such as patients on antihypertensive therapy with a history of hypotension, or elderly patients.[1,3-5,29] [See 'Volume depletion]
Lithium	The general relevance of an isolated case report of a **decreased lithium concentration** in one patient after starting empagliflozin is uncertain[44], however the prescribing information for some SGLT2 inhibitors cautions that the concomitant use of an SGLT2 inhibitor with lithium may decrease serum lithium concentrations[1,3,4].	It is advised to monitor serum lithium concentrations more frequently after SGLT2 inhibitor initiation or dose changes.[1,3,4]
Digoxin	Canagliflozin **may increase serum digoxin** concentrations[3,44,45], probably due to inhibition of P-glycoprotein[3,44].	Standard routine monitoring of digoxin concentrations should identify any interaction.[45]
Dabigatran	Canagliflozin (a weak P-glycoprotein inhibitor) **may** increase dabigatran concentrations.[3]	The manufacturer advises to monitor for signs and symptoms of bleeding if given concurrently.[3]
UGT enzyme inducers	Concomitant administration of UGT enzyme inducers (e.g., rifampicin, phenytoin) **might cause reduced exposure** to empagliflozin and canagliflozin.[3,4]	Monitoring of glycaemic control in T2DM is recommended[3,4] and the SmPC of canagliflozin provides guidance on a canagliflozin dose adjustment[3].

*UGT = UDP-glucuronosyltransferases; *Consult the SmPC for the full licensed prescribing information, available at www.hpra.ie or www.medicines.ie*

Monitoring parameters

In addition to monitoring of glycaemic indices in those with T2DM (in line with their regular diabetes reviews), renal function and volume status (e.g., weight, blood pressure) should be monitored at baseline and periodically during treatment with SGLT2 inhibitors[17], following standard HF and/or CKD monitoring guidance.

Initial decline in eGFR [See also 'Volume depletion']

Of note, there may be an initial small, reversible decline in eGFR within the first few weeks after commencing treatment with SGLT2 inhibitors[6,26,34], resulting from changes to the blood flow in the kidneys with a small reduction in the blood flow going through the glomeruli[26]. **This expected reversible dip in eGFR is not associated with progressive reduction in kidney function or acute kidney injury**[13] **and is not an indication to discontinue therapy**[26,27]. If an individual has a kidney function assessment within the first few weeks post initiation of an SGLT2 inhibitor, a decline in eGFR needs to be interpreted with caution and in the context of an expected drug effect, in order to avoid unwarranted discontinuation of treatment.[6] Extra monitoring is not generally required unless the person is unwell or starting another drug likely to impact renal function.[31]

Additional information to discuss with a person starting an SGLT2 inhibitor

'Sick day' guidance

People being initiated on an SGLT2 inhibitor should be provided with 'sick day' guidance[6,37] outlining what they should do if they become unwell and dehydrated, and **this guidance should be reiterated at every review**[6,34]. Advise people that they should **temporarily** stop their SGLT2 inhibitor if acutely unwell, especially if experiencing vomiting or diarrhoea, restricted food intake (e.g., fasting before an elective surgical procedure) or dehydration.[6] Treatment with SGLT2 inhibitors should be restarted when the person's condition has recovered and they are eating and drinking normally[6] (usually after 24 to 48 hours of eating and drinking normally[46]).

Perioperative management

The main concern about the perioperative use of SGLT2 inhibitors is the development of DKA and particularly euglycaemic DKA and ketoacidosis **in those with or without diabetes mellitus**.[47] The benefits of holding SGLT2 inhibitors preoperatively to prevent DKA, must be weighed against the potential deterioration in glycaemic control, and a reduction in cardiac and renal function.[48]

It was thought that euglycaemic ketoacidosis in people without diabetes taking SGLT2 inhibitors was unlikely and there was an argument for them to be continued perioperatively, however, there have been a small number of case reports of SGLT2 inhibitor-induced euglycaemic ketoacidosis in this group of patients.[48]

Due to a limited evidence base, there remains uncertainty about the **optimal** perioperative management of patients taking SGLT2 inhibitors[47], however current guidance is that **SGLT2 inhibitors should be omitted the day before and the day of elective surgery**.[47,48]

A multidisciplinary consensus statement synthesises the existing evidence on the elective perioperative management of adults taking SGLT2 inhibitors and provides practical recommendations to support clinicians and patients.[47]

Monitor ketone levels during SGLT2 inhibitor treatment interruption in patients who have been hospitalised for major surgery; measurement of **blood ketones** is preferred to urine.[8,48]

People should be counselled on how to manage their SGLT2 inhibitor if they become unwell postoperatively after they have been discharged.[48]

Practical aspects

Adults with swallowing difficulties

SGLT2 inhibitor tablets are film-coated but can be crushed (off-label except for ertugliflozin) and mixed with water or given with soft food.[49]

Missed doses

Dapagliflozin, empagliflozin or ertugliflozin

- If it is 12 hours or more until the next dose: take the dose as soon as it is remembered and then continue with the next dose at its usual time.[1,4,5]
- If it is less than 12 hours until the next dose: skip the missed dose and take the next dose at the usual time; do not take a double dose to make up for the forgotten dose.[1,4,5]

Canagliflozin

- If a dose is missed it should be taken as soon as the person remembers, however if it is nearly time for the next dose the missed dose should be skipped; a double dose should not be taken.[3]

Important counselling points and reminders for people taking SGLT2 inhibitors

- 'Sick day' guidance to be followed if unwell; remind at every medication review.[6,34]
- Educate on the risk of fungal genital infections such as thrush and ensure the person has a good understanding of the importance of genital hygiene.[6,34]
- Counsel on the symptoms of Fournier's gangrene (severe pain, tenderness, erythema or swelling in the genital area accompanied by fever/malaise), and to stop their SGLT2 inhibitor and seek urgent medical attention should they develop such symptoms.[6]
- People also taking diuretics should be counselled on the symptoms of hypovolaemia and advised to seek medical attention should they develop such symptoms.[6]
- People with diabetes should be counselled on routine preventative foot care.[1,31]
- Advise about the symptoms of UTI[28,50] and that effective prompt management of these infections should be undertaken[26].

The choice of agent and dose should always be specific to each individual patient based on their medical history, preferences and concomitant medicines; the guidance above should be considered in consultation with the licensed product information in the relevant Summary of Product Characteristics (SmPC). Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. Our full list of references can be accessed via the Reference List button.

Reference List

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