MIL

Oxford University Hospitals NHS
NHS Foundation Trust

Use of sodium-glucose co-transporter 2 inhibitors (SGLT2i) in adults

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Introduction

SGLT2i are indicated in type 2 diabetes, chronic kidney disease and heart failure. They may need to be suspended in patients with limited oral intake (e.g. peri-operatively).

Management

Indications

Heart failure

- EF over 40%: In combination with MRA
- EF 40% or less: In combination with β-blocker, MRA, & RAS inhibitor (or sacubitril / valsartan)

T2DM

- As per NICE guidance
- CKD (eGFR 15-90)
- Heart failure (any)
- History of vascular disease*
- Aged 40 yrs or over & QRISK greater than 10%
- Aged under 40 yrs & 1 or more risk factors**

CKD

- T2DM & eGFR 15-90
- If at risk of CKD progression:
  - eGFR less than 45
  - eGFR 45-90 & proteinuria***

Indicated

Contraindications

Contraindications

- Pregnancy or breastfeeding
- T1DM
- T2DM **WITH** history of DKA, insulin deficiency, ketogenic diet or recurrent/problematic hypoglycaemia
- Other non-T2DM diabetes

Cautions

- Systolic blood pressure less than 95 mmHg
- Consider reducing diuretic doses when starting
- Recurrent UTI
- Renal transplant / immunosuppressed patients

None/benefit outweighs risk

Dosing

Dapagliflozin 10mg once daily if eGFR 15 or more

Empagliflozin 10mg once daily if eGFR 20 or more
(NB: in T2DM can increase to 25mg once daily if needed & eGFR over 60)

*Established coronary artery disease/revascularisation, acute coronary syndrome, cerebrovascular disease, peripheral artery disease
**hypertension, dyslipidaemia, smoking, obesity, first degree relative with premature cardiovascular disease
***Urine albumin:creatinine ratio over 22.6mg/mmol OR protein:creatinine ratio over 35mg/mmol

Definitions

CKD	Chronic kidney disease
DKA	Diabetic ketoacidosis
eGFR	Estimated glomerular filtration rate; units are mL/min/1.73m^2
MRA	Mineralocorticoid receptor antagonist
QRISK	Cardiovascular risk calculator. QRISK2 or QRISK3 are acceptable
RAS	Renin-angiotensin system
T1DM/T2DM	Type one or two diabetes mellitus
UTI	Urinary tract infection

Safe use (all patients)

Patient Information	Patient Information Leaflet should be given to all patients starting SGLT2i (or pasted into the discharge letter). This can be found here.

Monitoring	• No additional bloods/checks required
	• T2DM: team normally managing patient's diabetes should non-urgently review diabetes medications (see below).
	• Counsel all patients on:
	  ○ Risk of dehydration
	  ○ Symptoms of DKA
	  ○ The importance of following 'sick day rules'

Drug Interactions	• Insulin or insulin secretagogues → hypoglycaemia • Antihypertensives → hypotension • Diuretics → hypotension; consider diuretic dose reduction, esp. if SBP less than 95mmHg

Significant ADRs	• Dehydration: Especially if on diuretics (consider reducing diuretic dose)
	• UTI: marginally increased risk (~7%) – caution in risk groups (renal transplant, abnormal urinary tract etc).
	• If type 2 diabetes increased risk of:
	  ○ Hypoglycaemia
	  ○ DKA (although still very rare; can be euglycaemic), especially if taking insulin.
	  ○ Genital tract fungal infection (treat with antifungal; no need to stop SGLT2i)
	  ○ Possible association with Fournier's gangrene (necrotising fasciitis of genitalia or perineum): advise to stop and seek medical advice if develops groin pain, tenderness, erythema, or swelling in the genital or perineal area associated with fever or malaise. Report via Yellow Card scheme
	• Peripheral Vascular Disease & Amputation risk: overall evidence does **not** suggest increased risk; SGLT2i should be withheld if acutely unwell.

Safe use in people with diabetes

Risk	Management
Hypoglycaemia	Consider the following adjustments to the patient's existing regimen, in consultation with the diabetes team: • Insulin: Reduce dosage by 20% • Sulfonylurea (e.g. gliclazide), meglitinide (e.g. repaglinide): Reduce dosage by 50% • Metformin ± pioglitazone ± DPP-4i/gliptins or GLP-1RA: No dosage adjustment necessary alternatively ask the GP or diabetes team to initiate SGLT2i

DKA	SGLT2i increase the risk of DKA in patients with diabetes. To reduce this risk particular care should be taken to withhold SGLT2i in some inpatients with diabetes – this includes the peri-operative period.
Lack of effect	Glucose lowering effect limited if eGFR 45

Withholding/delaying initiation of SGLT2i (ALL patients)

- If unwell/perioperative and on SGLT2i, consider monitoring ketones daily.

WITHHOLD OR DELAY INITIATION IF:	WHY?
• Nil by Mouth (NBM) • Surgery planned or likely to occur – withhold 24 hours prior • Dehydration risk • Vomiting • Choosing to intermittently fast (e.g. Ramadan)	Increased risk of DKA; can be euglycemic; highest risk if: • Requiring Insulin • Rapid progression to insulin (less than 1 year) • HbA1c greater than 86 mmol/mol • History of DKA • Lower BMI (less than 27kg/m^2) • Excess alcohol consumption • Pancreatic disease e.g. pancreatitis

Restarting SGLT2i

- For inpatients, ideally commence/restart when patient well, and eating and drinking normally, and they have recovered from acute illness/no surgery is imminently planned.
- Alternatively, prescribe on discharge summary if about to be discharged.
    - If you want to continue to hold SGLT2i on discharge: ADD to TTO list by prescribing & changing 'Dose Change Reason' from N/A to 'Suspended' – include a (re)start plan in 'Special Instructions'.

End of MIL table

Prepared by	Review date	Further information
Doreen Zhu, Michael Turner, Jame McCrae, Paul Clarke, James Gamble	Oct 2028	NICE guidance - Heart failure - - T2DM UK Kidney Association guidelines - SGLT2i in kidney disease