Practical approach to SGLT2 inhibitors for treatment of cardiovascular disease

Indications

Patients with Type 2 DM[1]

or

Patients with chronic kidney disease (eGFR 25-90, UACR>20 mg/mmol)[2]

or

Patients with chronic HFrEF[3]

Contraindications

- CLI[3]
- eGFR<25[4]
- Allergy or intolerance to SGLT2i[5]

→ Do not initiate SGLT2i

Caution

- Volume depletion[5]
- Active GMI[6]
- Hypotension (Blood pressure<95 mmHg)[*, 7]
- Prior CLI
- DKA[5] [specific to DM]
- History of severe hypoglycemia[†] [specific to DM]

→ Delay initiation of SGLT2i until condition resolved/ therapies modified to reduce risk

Outpatient Initiation

Start 10 mg od qam:

- Dapagliflozin[5]
- Empagliflozin[8]

Start 100 mg od qam:

- Canagliflozin[9]

Special Considerations

- Monitor for GMIs, counsel on proper hygiene[6]
- Concomitant dehydrating illness (SADMANS)[‡,10]
- Borderline renal function[§, 5, 6]
- Volume depletion[‖,5]

Potential drug-drug effects with:

Loop diuretics

- Optional dose reduction[¶] if euvolemic; 30–50% dose reduction if volume depletion occurs[3]

Insulin or SU

- If DM w/A1C<7.5, consider dose reduction (i.e., 10–20% insulin, and/or 50% SU)[11]
- If episodes of hypoglycemia[#], stop SU and dose reduce insulin[11]

Follow-up

Follow up routine as per underlying condition:

- Weight[6]
- Symptoms of hypotension[6]
- Adherence[6]
- Renal function (eGFR)[**, ††, 6]
- Blood glucose[6] [specific to DM]

Abbreviations:

CLI: critical limb ischemia; **DKA:** diabetic ketoacidosis; **DM:** diabetes mellitus; **eGFR:** estimated glomerular filtration rate; **GMI:** genital mycotic infections; **HFrEF:** heart failure with reduced ejection fraction; **SGLT2i:** SGLT2 inhibitors; **SU:** sulfonylurea; **UACR:** urine albumin to creatinine ratio

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Sick Day Medication List:

Patient becomes ill and is unable to maintain adequate fluid intake or have an acute decline in renal function (e.g. dehydrating illness)

S: sulfonylureas
A: ACE inhibitors/angiotensin or angiotensin neprilysin inhibitors
D: diuretics, direct renin inhibitors

M: metformin, mineralocorticoid receptor antagonists
A: angiotensin receptor blockers
N: nonsteroidal anti-inflammatory
S: SGLT2 inhibitors*

* Decompensated heart failure does not count as a sick day for this drug, even if hospitalized, unless cardiogenic shock or acute kidney injury is present

Abbreviation: **ACE:** angiotensin-converting-enzyme

Footnotes:

***** Hypotension includes SBP <90 or significant symptomatic hypotension[12]; **†** Defined as any hypoglycemia requiring assistance of another person (this is typically a plasma glucose level of <2.8 mmol/L but can occur at higher readings)[13]; **‡** See sick day meds above; **§** Check creatinine in 2-4 weeks; **‖** When applicable, reduce furosemide[3]; **¶** Most patients on concomitant diuretic dose do not undergo change in dose[3]; **#** If DM with repeated hypoglycemic episodes (outside of an acute illness with continued medication or in absence of obvious causes), refer to endocrinology; ****** Expected 15% drop in eGFR early, concern only if drop >25% from baseline, first option reduction/hold diuretic[3]; **††** If renal function declines (notably in macroproteinuric patients), other nephrotoxins (i.e., RAAS blockers, NSAIDS, etc.) must be ruled out and volume depletion must be corrected before consideration of holding SGLT2i. Consider holding medication and consult nephrology if GFR reduces by > 30%.[5] Not currently indicated in Canada for Type I DM

Abbreviations: **NSAIDS:** nonsteroidal anti-inflammatory drug, **RAAS:** renin-angiotensin-aldosterone system, **SBP:** systolic blood pressure

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