Initiation of SGLT2 Inhibitors in Patients with Heart Failure

1. Assess Fluid Status
2. Check baseline Blood Pressure and Biochemistry
3. Determine Diabetes History

1. Assessment of fluid status by specialist team when addition of SGLT2i to diuretic therapy	
Volume status of patient	**Changes to existing therapy**
Euvolaemic patients	*Consider* dose reduction of loop diuretic by equivalent of Furosemide 40mg if appropriate
Volume overload	Add SGLT2i to existing diuretics
Hypovolaemia	Correct volume depletion before considering
Thiazide diuretic for hypertension	Discontinue the thiazide diuretic and replace with SGLT2i – review BP in 4-6 weeks and initiate or titrate alternative antihypertensive. Preference should be to up titrate ACE/ARB/ARNI, beta blockers and MRAs
Thiazide in combination with a loop for fluid overload	Discuss with cardiologist

2. Assessment of Blood Pressure and Biochemistry	
Blood Pressure	SGLT2i not recommended if symptoms of hypotension or a SBP<95mmHg
Urea and Electrolytes	Dapagliflozin contraindicated if eGFR<15 ml/min/1.73m^2 Empagliflozin contraindicated if eGFR<20 ml/min/1.73m^2

Patients with moderate-severe LVSD and T2DM

Non-diabetic patients with moderate-severe LVSD

3. Patients with T2DM and HF: Addition of SGLT2i to other glucose lowering medication	
Current diabetic status	**Advice**
On metformin monotherapy or diet	Add SGLT2i
HbA1c 48-60 on 2-3 antidiabetic agents (metformin, DPP-4 inhibitor or GLP-1)	Stop DPP-4 inhibitor and add SGLT2i
HbA1c >60 on 2-3 antidiabetic agents (metformin, DPP-4 inhibitor or GLP-1)	Add SGLT2i to existing therapy (could consider stopping DPP-4 inhibitor)
HbA1c >78	Ask primary care diabetes clinic to assess suitability and consider referring to secondary care if this is indicated
Patients on sulphonylureas (SU)	Ask primary care diabetes clinic to consider initiating
Patients on insulin	Refer to Endocrine due to risk of hypoglycaemia (via HF MDT)
NOTE: Patients with eGFR < 45 ml/min/1.73m^2. Little benefit is gained in terms of diabetic control as the mechanism of action for glucose management is significantly reduced. If eGFR falls below 45ml/min/1.73m^2, additional glucose lowering therapy may need to be considered.	
SGLT2 inhibitors are NOT RECOMMENDED for treatment of HF in patients with Type 1 Diabetes	

If clinically appropriate start **Dapagliflozin 10mg daily** or **Empagliflozin 10mg daily and provide full patient counselling**

- Patients with severe hepatic impairment, Dapagliflozin 5mg daily, increasing to 10mg daily if tolerated
- Empagliflozin is not recommended in severe hepatic impairment

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Key

SU – Sulphonylurea e.g. gliclazide, glipizide

DPP-4 inhibitors – dipeptidyl peptidase 4 inhibitors e.g. sitagliptin, linagliptin, saxagliptin, alogliptin

GLP-1 – glucagon-like peptide 1 receptor agonists e.g. dulaglutide, liraglutide, exenatide, semaglutide,

Monitoring

- Reassess volume status, BP and U&Es in 2-4 weeks. If Diabetic re-check HbA1c in 3–6 months.
- eGFR is known to dip slightly after initiation but SGLT2 inhibitors are reno-protective
- Assess renal function at least yearly, thereafter and prior to initiation of concomitant medicines that may reduce renal function and periodically thereafter
- Monitor fluid balance regularly, particularly when a patient is taking diuretics, is old and/or frail
    - SGLT2 inhibitors may intensify diuresis, particularly when accompanied by sacubitril/valsartan and diuretic therapy
    - Diuretic doses along with fluid intake should be balanced in order to avoid dehydration, symptomatic hypotension and prerenal failure
    - Elderly and frail patients are at particular risk of developing these complications
- Monitor glycaemia regularly, particularly when a patient is diabetic and consider modification of other diabetic medicines

Patient Counselling

- Provide patient information leaflet Forxiga PIL (AstraZeneca) Jardiance PIL (Boehringer Ingelheim) and sick day rules card
- Polyuria – seek advice if signs of dehydration e.g.thirsty, dark urine, dry mouth
- Fungal genital infections (thrush) and UTIs are common in patients with Type 2 DM
    - Most cases are mild to moderate and can be managed with a short course of antifungal cream or oral treatment
    - Emphasise importance of good personal hygiene (genital/perineal)
    - Those with prior history are more likely to have recurring infection
- Risk of orthostatic hypotension
- Discuss signs and symptoms of DKA (risk in non-diabetic population is low)
- Sick Day Rules – advise patients if they have an acute dehydrating illness, infection or are undergoing surgery to temporarily withhold SGLT-2 inhibitor then RESTART when eating and drinking normally

Sick Day Rules for avoiding or recognising DKA (If a patient has a history of DKA, consider discussion with diabetes team prior to initiation)

There are several classes of drug that should be stopped if the patient is at risk of dehydration due to acute illness.

S	SGLT-2 Inhibitors	Increased risk of euglycaemic DKA
A	ACE Inhibitors	Increased risk of AKI due to reduced renal efferent vasoconstriction
D	Diuretics	Increased risk of AKI
M	Metformin	Increased risk of lactic acidosis
A	ARBs	Increased risk of AKI
N	NSAIDs	Increased risk of AKI due to reduced renal efferent vasoconstriction

Signs and Symptoms of DKA

- Excessive Thirst
- Polyuria
- Dehydration
- Rapid weight loss
- Shortness of Breath and laboured breathing
- Abdominal pain
- Leg Cramps
- Nausea and Vomiting
- Mental confusion and drowsiness
- Ketones can be detected on the person's breath (pear-drop smell) or in the blood or urine

References:
2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: Supplementary data..
Forxiga (Dapagliflozin) Summary of Product characteristics. Available at www.medicines.org.uk/emc (accessed 16/3/22)
Jardiance (Empagliflozin) Summary of Product characteristics. Available at www.medicines.org.uk/emc (accessed 02/06/22)