

Prescribing guide for the initiation of dapagliflozin for heart failure

Introduction

Dapagliflozin has been shown to improve patient's symptoms, reduce hospitalisations and reduce mortality associated with heart failure in those with reduced ejection fraction. This effect was seen in those with and without diabetes.

The following guide is to support safe introduction of dapagliflozin for the **management of heart failure** – this is not a comprehensive guide for the management of glycaemic control in those with diabetes.

Following results for the DAPA HF trialⁱ, local formulary application and a NICE TAⁱⁱ the following criteria should be met for considering initiating dapagliflozin as an option to treat heart failure:

- Optimum medical management with ACE (ARB or ARNI), BB, MRA
- Ejection Fraction less than 40%
- Symptomatic – NYHA II and above

Formulary Status – Primary Care

The NICE TA for dapagliflozin for the treatment of symptomatic heart failure with reduced ejection fraction ([NICE TA 679](#)) states that dapagliflozin should be started on the advice of a heart failure specialist.

In Primary Care across TNW (Tower Hamlets, Newham and Waltham Forest) dapagliflozin use in heart failure holds amber status and can be initiated at the recommendation of a specialist.

Further information / considerations:

Diuretics - due to the mechanism of action, additional diuresis should be expected when adding dapagliflozin to therapy. It should be noted that within the DAPA trial there was no mandate to amend diuretic therapy and a paperⁱⁱⁱ reviewing diuretic doses supports the advice to maintain diuretic therapy when adding dapagliflozin then to titrate diuretics according to response as per standard practice.

Blood pressure can be affected by dapagliflozin due to the diuretic action and a slight reduction in blood pressure expected. In keeping with other agents in the treatment of heart failure it is prudent to ensure systolic blood pressure is above 100mmHg when initiating. Should this be lower once initiated, but the patient is tolerating hypotension, then it should continue.

Renal function - Within the trial (and license), **in the treatment of heart failure**, creatinine clearance at initiation is to be >30ml/min. In the treatment of diabetes, given the required action is excretion of glucose and sodium from the kidneys, the creatinine clearance is crucial for its blood glucose lowering effects and indeed clearance is to be above 60ml/min for

initiation and maintained above 45ml/min for it to continue – the rationale is that as the GFR reduces, the effectiveness at excreting glucose and sodium reduces.

In the treatment of heart failure in a diabetic patient, dapagliflozin can be added despite GFR being less than 45ml/min on the understanding that the drug is added for **benefits in heart failure and NOT for glycaemic control**. On initiating dapagliflozin, there can be an initial decline in renal function (a drop in creatinine clearance of up to 5ml/min has been observed in the DAPA trial) but longer term it prevents further decline when compared to the placebo group.

Diabetes – for the management of diabetes, the SGLT2 inhibitors act to increase urinary glucose and sodium excretion. This action is related to baseline levels and as such in those patients with poor control, you are likely to see relatively large reductions in absolute HbA1c. For individuals well controlled or for those without diabetes, the drop in HbA1c is negligible and as such there should be confidence when adding dapagliflozin to existing therapy for diabetes with the exception of patients on insulin and/or sulphonylureas, as detailed below.

In those with type 2 diabetes mellitus, there is a small increased risk of diabetic ketoacidosis (DKA) of between 1/1,000 to 1/10,000^{iv} – this is similar to the risk of angioedema in ACE inhibitors.

For patients with increased risk of DKA – dapagliflozin use in heart failure should be **avoided** and includes:

- those with type 1 diabetes
- those on a ketogenic diet and those who may have previously had DKA

Additionally oral agents that increase insulin secretion such as sulphonylureas should be halved when adding dapagliflozin and in the first instance those with type 2 diabetes on insulins discussed with the diabetic team to oversee introduction if deemed appropriate (again dosing of insulin to be adjusted if adding dapagliflozin).

Patient counselling – Tailored according to co-morbidities (i.e. with or without type 2 diabetes) – also note there are two informative leaflets available to download from the company at: <https://www.forxiga.co.uk/heart-failure.html>

Patients will note increased diuresis and as there is more glucose in the urine there is an increased risk of getting genital infections such as thrush – 1 in 10 for females and 1 in 20 for males, for this reason good genital hygiene is strongly encouraged.

Additional counselling for those with type 2 diabetes:

For those with type 2 diabetes, give awareness of sick day rules - if you are too unwell to eat or drink then stop taking dapagliflozin until you feel recovered. Should they have an acute illness and exhibit signs symptoms of DKA such as: excessive thirst, feeling and/or being sick, rapid weight loss, deep sighing breathing, stomach pain, drowsiness and sweet-smelling breath (like pear drops or acetone) – seek immediate medical attention.

Where dapagliflozin is co-prescribed with sulphonylureas or insulin, 1 in 10 patients will experience low blood sugar levels, signs and symptoms include; shaking, sweating, feeling anxious, fast heart rate, feeling hungry, headache, change in vision, change in mood or feeling confused. Cautious introduction with dapagliflozin should be done when co- prescribing with these agents to prevent hypoglycaemia – reducing sulphonylurea dose and insulin doses by half is recommended when initiating.

As dehydration is to be avoided when taking dapagliflozin, caution should be had in periods of excessive heat and during periods of fasting – i.e. if required to go nil by mouth prior to operations – dapagliflozin is to be withheld.

Abbreviations

ACEi	Angiotensin-converting enzyme inhibitor
ARB	Angiotensin receptor blockers
ARNI	Angiotensin receptor neprilysin Inhibitor
BB	Beta Blocker
MRA	Mineralocorticoid receptor antagonists
NYHA	New York Heart Association – <i>functional classification for heart failure</i>

ⁱ McMurray JJV, Solomon SD, Inzucchi SE et al. Dapagliflozin in patients with heart failure and reduced ejection fraction . *NEJM*. 2019; **381**: 1995-2008

ⁱⁱ NICE TA679 – Dapagliflozin for treating chronic heart failure with reduced ejection fraction. Available at <https://www.nice.org.uk/guidance/ta679>

ⁱⁱⁱ Jackson AM and Murray JJV, Dapagliflozin and diuretic use in patients with heart failure and reduced ejection fraction in DAPA-HF. *Circulation*. 2020; **142**: 1040-54

^{iv} Summary of Product Characteristics – Forxiga (Dapagliflozin) available at [last accesses 19/4/21] <https://www.medicines.org.uk/emc/medicine/27188>