Information for prescribing Dapagliflozin in Heart Failure for Primary Care and Non-specialists

This document to support the use of dapagliflozin in heart failure for patients who are either non-diabetic or those with type 2 diabetes.

Indications [1]	Dapagliflozin is a licensed sodium-glucose transport protein 2 (SGLT2) inhibitor option for adult patients with heart failure NYHA class II-IV [2]. It is recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction in adults, **only if it is used as an add-on to optimised standard care with**[2]: • angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), or • sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.
Dose [1]	The recommended dose is 10 mg dapagliflozin once daily. Dapagliflozin in heart failure is a Green drug and it should be initiated under the advice of a heart failure specialist in hospital, community or by a GP with Specialist Interest. When dapagliflozin is used in combination with insulin or an insulin secretagogue, such as a sulphonylurea, a lower dose of insulin or insulin secretagogue may be considered to reduce the risk of hypoglycaemia[1].
Contraindications [1]	• History of diabetic ketoacidosis (DKA) • Severe renal impairment with an eGFR < 15 ml/minute/1.73m^1 or end stage renal disease or dialysis patients • Pregnancy or breastfeeding • Type 1 diabetes (known or suspected)
Cautions [1]	• Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and as such may increase the risk of dehydration and hypotension. Depending on clinical condition, diuretic dosage may need to be reduced on initiating dapagliflozin. • There is limited experience with dapagliflozin for the treatment of heart failure in patients with severe renal impairment (GFR < 25 mL/min). • No dose adjustment is necessary for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, a starting dose of 5 mg is recommended. If well tolerated, the dose may be increased to 10 mg when indicated [1]. • Pregnancy- dapagliflozin is not recommended as treatment options during the second and third trimester of pregnancy. • Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses which cause acute inflammation or if there is a severe infection or sepsis. Further information overleaf.
Monitoring [1]	See table overleaf
Specialist responsibilities [1] (including specialists within the hospital and community heart failure services where available)	Before or on initiation, the specialist should: • Ensure that the patient is able to access the "Your guide to Forxiga ®" information: https://www.forxiga.co.uk/content/dam/open-digital/forxiga-uk-redesign/en/pdf/Forxiga-HeartFailure-PatientBooklet.pdf • If using dapagliflozin for patients with type 2 diabetes as a co-morbidity: - Risk assess the patient for diabetic ketoacidosis (DKA) and ensure ketone levels are normal. Treatment should not be started until ketone levels are normal. - Patients should be informed of the risk and risk factors of DKA and how to recognise signs, symptoms. Recommend stopping in line with the Sick Day Rule. - Consult with the diabetes team for further information or support if needed.
Primary care responsibilities [1] under the advice of specialist heart failure teams in the hospital or Community	**Key roles to be undertaken in primary care following a recommendation from secondary care:** • Monitor renal function every 3 to 6 months depending on risk • Report to and seek advice from the specialist on any aspect of patient care, which is of concern and may affect treatment.

The manufacturer's summary of product characteristics (SPC) and the most current online edition of the British National Formulary should be consulted for full information on contraindications, warnings, side effects and drug interactions.

References

1. Summary of Product Characteristics *Forxiga 10 mg film-coated tablets* AstraZeneca UK Limited 10 Nov 2021. Accessed 29/04/2022 https://www.medicines.org.uk/emc/product/2865/smpc#gref
2. National Institute of Clinical and Health Excellence (NICE) *Dapagliflozin for treating chronic heart failure with reduced ejection fraction Technology appraisal guidance [TA679]* Published 24/02/2021. Accessed 07/05/2021 https://www.nice.org.uk/guidance/TA679

MONITORING		
	Parameter	**Frequency**
	In addition to absolute values for haematological indices, a rapid fall or rise and a consistent upward or downward trend in any value should prompt caution and extra vigilance	
Specialist/ Primary care	Urea & Electrolytes (U&Es) including creatinine	• Prior to starting treatment and 4 weeks after initiation • Then 3-6 months depending on their eGFR if <60 mL/min/1.73m^2. As a minimum renal function should be checked annually if ≥60 mL/min/1.73m^2. • Prior to, and after, initiation of concomitant medicinal products that may reduce renal function.
	Blood pressure	• Prior to starting and 4 weeks after initiation • Before starting a new antihypertensive or initiating/increasing/decreasing doses of a diuretic
	Symptoms	**Action for GP to take if symptom occurs**
Non-specialists and Primary Care	Volume depletion	Dapagliflozin has a known diuretic effect • During initiation: consider reducing or holding the patients diuretics. • During continuation: Monitor and consider reducing or stopping other diuretics
	Renal dysfunction	• During initiation: There may be a temporary increase in creatinine or reduction in the eGFR which is expected. Continue monitoring in line with the guidance. / • Continuation- only consider stopping if eGFR < 20 ml/minute/1.73m2
	Hypoglycemia	• This is rare in non-diabetics. Stop dapagliflozin and refer to the heart failure team for advice to manage heart failure. • If the patient has type 2 diabetes, seek advice from the local diabetes team.
	Genital mycotic infections and UTI's	• Withhold dapagliflozin until severe infection has resolved
	Temporarily withhold dapagliflozin (or any other SGLT2 inhibitor) in patients who • are hospitalised for major surgery or acute serious illnesses - In hospital, blood ketone levels should be monitored in type 2 diabetic patients only (and be normal before restarting) • are not eating and drinking • admitted for elective surgery/procedure requiring starvation • have vomiting or diarrhoea (or any inter-current conditions that may lead to volume depletion) • have major infection (i.e. pyelonephritis or urosepsis) • Acute inflammation, infection or sepsis. Restart once the acute episode is resolved	• Withhold dapagliflozin and restart when the patient is better and is eating and drinking
	Diabetic Ketoacidosis (DKA) Type 2 diabetics only - non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.	Primary Care: • If the patient is symptomatic, stop the SGLT2 inhibitor for 3-5 days in line with the 'Sick Day Rule'. If the patient continues to be symptomatic, contact the diabetes team for additional support and advice. If in hospital: • Conduct a **blood** ketone test, regardless of blood glucose level. Do not take a urine ketone test • If DKA identified, interrupt dapagliflozin treatment and monitor until levels return to normal and consider restarting once the patient has stabilised and the acute episode is over.

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