Amber with Guidance = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
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Barnsley Hospital NHS Foundation Trust | South West Yorkshire Partnership NHS Foundation Trust | South Yorkshire Integrated Care Board

SGLT2 Inhibitors: Dapagliflozin (Forxiga®) and Empagliflozin (Jardiance®) for Heart Failure with reduced Ejection Fraction (HFrEF) and Dapagliflozin (Forxiga®) for Heart Failure with preserved ejection fraction (HFpEF)

Please note: Dapagliflozin and Empagliflozin are to be initiated by a cardiology specialist/cardiologist and communicated to both primary care and the community heart failure team.

Should a patient require referral back to a cardiologist, please refer back to the initiating consultant.

Background Information	In February 2021, NICE TA679 was published providing evidence-based recommendations on the use of dapagliflozin for symptomatic chronic heart failure with reduced ejection fraction in adults. In March 2022, NICE TA773 was published evidence-based recommendations on the use of empagliflozin for symptomatic chronic heart failure with reduced ejection fraction in adults. Both Empagliflozin and Dapagliflozin are 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: - 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. In June 2023, NICE TA902 was published providing recommendations for dapagliflozin for treating symptomatic heart failure with preserved or mildly reduced ejection fraction in adults.	
BNF therapeutic class	Blood glucose lowering drugs > Sodium glucose co-transporter 2 inhibitors	
Indication	For the treatment of adults with symptomatic chronic heart failure.	
Dosage and administration	The recommended dosage for dapagliflozin is 10mg ONCE daily. **Renal Impairment:** No dose adjustment is required based on renal function, though there is limited experience with dapagliflozin for the treatment of heart failure in patients with severe renal impairment (GFR <30mL/min). In patients treated with dapagliflozin for both heart failure and type 2 diabetes mellitus, additional glucose-lowering treatment should be	The recommended dosage for empagliflozin is 10mg ONCE daily. **Renal Impairment:** When used for symptomatic chronic heart failure, in patients with or without type 2 diabetes mellitus, avoid if eGFR less than 20 mL/minute/1.73 m2. **Hepatic impairment:** No dose adjustment is required for patients with hepatic impairment.

	considered if GFR falls persistently below 45mL/min. **Hepatic Impairment:** No dose adjustment is necessary for patients with mild or moderate hepatic impairment. In those with severe hepatic impairment, a starting dose of 5mg is recommended. If well tolerated, the dose may be increased to 10mg where indicated. **Patients with type 1 diabetes mellitus:** Dapagliflozin is not recommended for the treatment of heart failure in patients with type 1 diabetes mellitus.	Empagliflozin exposure is increased in patients with severe hepatic impairment. Therapeutic experience in patients with severe hepatic impairment is limited and therefore not recommended for use in this population and should be avoided. **Patients with type 1 diabetes mellitus:** Empagliflozin is not recommended for the treatment of heart failure in patients with type 1 diabetes mellitus.
Cautions and Contraindications	**Cautions:** • Patients who a dapagliflozin-induced drop in blood pressure could pose a risk, such as patients on anti-hypertensive therapy with a history of hypotension or elderly patients. • Patients with increased risk of DKA (e.g. Type 1 and 2 diabetes patients with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis). • Cardiac failure – experience with dapagliflozin in NYHA class IV is limited • Raised haematocrit • Risk of volume depletion – correct depletion before starting treatment **Contraindications:** • Pregnancy: not recommended during the second and third trimesters of pregnancy and if pregnancy is detected, treatment with dapagliflozin should be discontinued. • Breast-feeding: A risk to the new born/infant cannot be excluded therefore dapagliflozin should not be used whilst breast-feeding.	**Cautions:** • Patients who an empagliflozin-induced drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older. • Patients with increased risk of DKA (e.g. Type 1 and 2 diabetes patients with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis). • Infiltrative disease or Takotsubo cardiomyopathy • Raised haematocrit • Risk of volume depletion especially in elderly patient aged 75 years and older - correct hypovolaemia before starting treatment. Consider interrupting treatment if volume depletion occurs. • Complicated urinary tract infections—consider temporarily interrupting treatment • Necrotising fasciitis of the perineum (Fournier's gangrene) • Lower limb amputations **Contraindications:** • Pregnancy: not recommended animal studies have shown

		adverse effects on postnatal development. As a precautionary measure, it is preferable to avoid the use of Empagliflozin during pregnancy. • Breast-feeding: A risk to the new born/infant cannot be excluded therefore Empagliflozin should not be used whilst breast-feeding.
Adverse Drug Reactions	**Very common (>1/10):** hypoglycaemia (when used with SU/insulin). **Common (>1/100 to <1/10):** genital infections, UTI, DKA (when used in T1DM), dizziness, rash, back pain, dysuria, polyuria, increased haematocrit, decreased renal clearance, dyslipidaemia. **Uncommon (>1/1000 to 1/100):** fungal infection, volume depletion, thirst, constipation, dry mouth, nocturia, genital pruritus, blood creatinine increased during initial treatment, blood urea increase, weight decreased. **Rare (>1/10,000 to <1/1000):** DKA (when used in T2DM). **Very rare (<1/10,000):** Necrotising fasciitis of the perineum (Fournier's gangrene) and angioedema.	**Very common (>1/10):** hypoglycaemia (when used with SU/insulin), volume depletion **Common (>1/100 to <1/10):** Vaginal moniliasis, vulvovaginitis, balanitis and other genital infection, UTI (including pyelonephritis and urosepsis), thirst, constipation, pruritus (generalised), rash, increased urination, serum lipids increased **Uncommon (>1/1000 to 1/100):** DKA, urticaria, angioedema, dysuria, blood creatinine increased/GFR decreased Haematocrit increased **Rare (>1/10,000 to <1/1000):** Necrotising fasciitis of the perineum (Fournier's gangrene) **Very rare (<1/10,000):** Tubulo-interstitial nephritis
Monitoring	Monitor renal function before starting treatment and at least annually thereafter. In case of intercurrent conditions that may lead to volume depletion (e.g. Gastrointestinal illness), careful monitoring of volume status (e.g. Physical examination, blood pressure measurements, laboratory tests including haematocrit and electrolytes) is recommended. Temporary interruption of treatment with dapagliflozin is recommended for patients who develop volume depletion until the depletion is corrected. Ketone monitoring is not routinely required for non-diabetic patients taking dapagliflozin for heart failure.	Monitor renal function before starting treatment and before initiation of concomitant drugs that may reduce renal function, then at least annually thereafter. In case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolytes is recommended for patients receiving empagliflozin. Temporary interruption of treatment with empagliflozin is recommended for patients who develop volume depletion until the depletion is corrected or those who develop complicated urinary tract infections until resolved.

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		Ketone monitoring is not routinely required for non-diabetic patients taking empagliflozin for heart failure.
Interactions	• Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics therefore increasing risk of dehydration and hypotension. • Increased risk of hypoglycaemia when using concomitant insulin or insulin secretagogues such as sulphonylureas.	• Empagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension • Insulin and insulin secretagogues, such as sulphonylureas, may increase the risk of hypoglycaemia.

Contact names and details

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References

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2. https://www.medicines.org.uk/emc/product/5441/smpc
3. https://www.nice.org.uk/guidance/ta679
4. https://www.nice.org.uk/guidance/ta773
5. https://bnf.nice.org.uk/drugs/dapagliflozin/

Development Process

This guidance has been produced following an AMBER-G classification status of Dapagliflozin (Forxiga®) and Empagliflozin (Jardiance®) for Heart Failure with reduced Ejection Fraction (HFrEF), and Dapagliflozin (Forxiga®) for Heart Failure with preserved ejection fraction (HFpEF) by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 11th October 2023.