Hertfordshire and West Essex adult (age≥18 years) treatment pathway
SGLT2 inhibitors for treating chronic heart failure based on NICE TA 679, 773, 902 and 929
AMBER INITIATION – recommended for restricted use - initiation by heart failure specialist, continuation in primary care

specialist heart failure teams (secondary care/community services)

Patient meets NICE initiation criteria in line with NICE TA 679 and NICE TA 773

Dapagliflozin and Empagliflozin are recommended as an option for treating symptomatic chronic heart failure with **reduced ejection fraction** (HFrEF) 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

Patient meets NICE initiation criteria in line with NICE TA 902 and NICE TA 929

Dapagliflozin and Empagliflozin are recommended, within its marketing authorisation, as an option for **treating symptomatic chronic heart failure with preserved or mildly reduced ejection fraction (HFpEF or HFmrEF)** in adults.

Patient selection by specialist heart failure teams (secondary care/community services)

Inclusion criteria
- HFrEF patients with ejection fraction <40% and NYHA II-IV
- Optimised on HF prognostic medications (ACE, ARB or ARNI, beta blocker and MRA if tolerated)
- eGFR ≥25ml/min for dapagliflozin, eGFR ≥20ml/min for empagliflozin
- No risk factors for developing diabetic ketoacidosis (DKA) (only applicable to diabetic HFrEF patients)

Inclusion criteria
- Patients with Left Ventricular Ejection Fraction (LVEF) > 40% and evidence of structural heart disease.
- NYHA II-IV
- eGFR ≥25ml/min for dapagliflozin, eGFR ≥20ml/min for empagliflozin
- No risk factors for developing diabetic ketoacidosis (DKA) (only applicable to diabetic chronic heart failure with preserved or mildly reduced ejection fraction patients)

Exclusion criteria
- eGFR <25ml/min for dapagliflozin, eGFR <20ml/min for empagliflozin
- Type 1 diabetic mellitus
- Hospital admission with DKA
- Ketosis prone diabetes (patients with pancreatic cancer/pancreatitis and patients who rapidly progressed to insulin treatment within 1 year of diagnosis)
- Ketogenic diet or eating disorder
- Conditions that lead to restricted food intake and severe dehydration
- Dapagliflozin/empagliflozin induced symptomatic hypotension
- Acute diabetic foot ulceration/acute foot ischaemia
- Hypersensitivity to dapagliflozin, empagliflozin or excipient, pregnancy & breastfeeding

Cautions for initiation
- Severe impaired hepatic function: dose adjustment may be required for dapagliflozin (a starting dose of 5 mg is recommended. If well tolerated, the dose may be increased to 10 mg), no dose adjustment for empagliflozin
- Frailty/cognitive impairment: increased risk of dehydration. Elderly patients are more likely to have impaired renal function and/or to be treated with anti-hypertensive medicinal products that may cause changes in renal function.
- Diabetes with HbA1c> 86mmol/mol: increased risk of dehydration due to osmotic symptoms; refer to diabetologist
- Patients on diuretics: increased diuresis; diuretic dose adjustments may be required

specialist heart failure teams (secondary care/community services)

Obtain **baseline assessment** including HBA1c, U&Es, LFTs, weight and volume status

NB: patients with type 2 diabetic mellitus (T2DM)

- Patients already on SGLT2-inhibitor; discuss with the patient's clinician responsible for diabetes care if a change to dapagliflozin or empagliflozin is warranted.
- Prior to initiating dapagliflozin/empagliflozin for chronic heart failure, the anti-diabetic effect dapagliflozin/empagliflozin must be considered amongst other concurrent anti-diabetes medications. Doses of other glucose-lowering therapy may need to be reduced prior to initiation. Patients treated with dapagliflozin/empagliflozin for both heart failure and type 2 diabetes mellitus, additional glucose-lowering treatment should be considered in patients with moderate renal impairment because glucose lowering efficacy is reduced and likely absent in patients with severe renal impairment. Patients may need to increase their frequency of blood glucose testing initially when dapagliflozin/empagliflozin is started to identify any resulting hypoglycaemia.
  - ❖ Patients on insulin, combination insulin/sulfonylureas, triple therapy, uncontrolled HbA1c or history of hypoglycaemia: refer to/discuss with specialist in diabetes care (in secondary care or community)
  - ❖ Patients on sulfonylureas, GLP-1 receptor agonists, repaglinide: refer to/discuss with the patient's clinician responsible for diabetes care
  - ❖ Patients on metformin, DPP-4 inhibitors (gliptins), acarbose: can be initiated by heart failure specialist team (secondary care/community services) as low hypoglycaemia risk

Initiation of therapy by specialist heart failure team & initial follow up

Inclusion criteria are met, cautions have been addressed, necessary adjustments to concurrent diabetic medication have been made (applicable to diabetic patients only)

The **recommended dose** of dapagliflozin/empagliflozin for heart failure is **10 mg once daily**. (dose reduction to 5mg for severe liver impairment for dapagliflozin). Initial prescription to be issued by specialist heart failure team

At initiation, discuss adverse effects and cautions for use including providing the following **information** to the patient:

- urine volume increase and risk of dehydration
- sick-days; suspend dapagliflozin if vomiting, severe sepsis and peri-operatively (inform prescriber)
- fungal genital infection and urinary tract infection
- avoidance of foot complications - suspend dapagliflozin if acute foot ulceration/ischaemia

Additional considerations for HFrEF/chronic heart failure with preserved or mildly reduced ejection fraction patients with T2DM:

- Counsel patients on symptoms of DKA and T2DM sick-day rules (temporarily stop if they are unable to eat and drink)

Patient information leaflet: available from Cardiology, Renal and Metabolic (CaReMe) group (an organisation of the following societies: Association of British Clinical Diabetologists, British Cardiovascular Society, The Renal Association, Primary Care Cardiovascular Society and Primary Care Diabetes Society). This is available on https://abcd.care/sites/abcd.care/files/site_uploads/Images/ABCD_A4_Leaflet_Final%20%28002%29.jpg
For complete list of adverse drug reactions; see SPC

Planned follow up for HFrEF, HFmrEF and HFpEF (virtual/clinic) :2-3weeks post initiation to include assessment fluid status, symptom review, where needed repeat U&E's & blood pressure. Adjust diuretic therapy if needed. Repeat assessment and follow up as needed for heart failure management.
Communicate to the GP clearly noting the indication for dapagliflozin/empagliflozin as HFrEF or chronic heart failure with preserved or mildly reduced ejection fraction and request addition to repeat prescription.

Primary care

Transfer prescribing to primary care: transfer information to include initial treatment and monitoring plan.
Once the patient is stable, in line with NICE guidance 108, 'chronic heart failure in adults' monitoring is required at least 6-monthly for stable patients with proven heart failure – including U&E's, renal function, fluid status and blood pressure.

Follow up for diabetic care (T2DM patients only): by the patient usual diabetic care provider.

Primary care

Stopping criteria

- Any of the exclusion criteria develop
- Patient experiences any serious adverse reaction e.g. ketoacidosis, angioedema, Fournier's Gangrene. (Yellow card to be submitted to the MHRA & record in patients notes)
- In patients with intercurrent illness if not eating or at risk of dehydration. Only restart once better and back on normal diet.
- In patients admitted to hospital acutely unwell for any reason. Restart only once fully recovered and eating and drinking normally.
- In any patient having elective surgery who is missing more than one meal. Restart only once recovered and eating and drinking normally

GP to contact heart failure specialist if concerns arise on contra-indications, stopping criteria, cautions and monitoring results

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Royal Free London NHS foundation Trust – Drugs and therapeutics committee, Dapagliflozin submission, 19th February 2021

Further information

1. SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis published 18th April 2016
2. SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation (mainly toes) published 22nd march 2017
3. SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) published 18th Feb 2019
4. SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness published 18th March 2020
5. SGLT2-2 inhibitor comparison document 'Sodium-glucose cotransporter-2 (SGLT2) inhibitors (Gliflozins) in Adults with Type 2 Diabetes (T2DM), accessed via https://www.enhertsccg.nhs.uk/endocrine-system

References consulted include:

1. Dapagliflozin for treating chronic heart failure with reduced ejection fraction, NICE TA 679, Published Feb 2021 https://www.nice.org.uk/guidance/TA679, accessed June 2021
2. Mc Murray et al., 'Dapagliflozin in patients with heart failure and reduced ejection fraction (Dapa-HF)', N Engl J Med 2019, 381(21):1995-2008
3. Forxiga 10 mg film-coated tablets, accessed via https://www.medicines.org.uk/emc/product/7607, June 2021
4. CaReMe heart failure algorithm November 2020, accessed via https://www.bsh.org.uk/wp-content/uploads/2020/12/CARE-HF-Algorithm-final-version-Nov-2020-1.pdf, June 2021
5. Chronic heart failure in adults: diagnosis and management, NICE guidance 106, published September 2018 https://www.nice.org.uk/guidance/ng106, accessed June 2021
6. Empagliflozin for treating chronic heart failure with reduced ejection fraction, NICE TA 773, Published March 2022 https://www.nice.org.uk/guidance/ta773, accessed April 2022
7. Packer M. et al, 'Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure (Emperor-Reduced)', N Engl J Med 2020, 383(15):1413-1424
8. Jardiance 10mg film-coated tablets, accessed via https://www.medicines.org.uk/emc/product/5441/smpc, April 2022
9. Dapagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction, NICE TA902, Published June 2023
10. Solomon S et al., 'Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (Deliver)', N Engl J Med 2022, 387:1089-1098
11. Empagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction, NICE TA929, Published November 2023
12. Anker S et al., 'Empagliflozin in Heart Failure with a Preserved Ejection Fraction (emperor-preserved)', N Engl J Med 2023, 385(16); 1451-1461

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Superseded version	Dapagliflozin & Empagliflozin for treating chronic heart failure with reduced ejection fraction based on NICE TA 679, 773 and 902 Pathway version 3.0 approved HWE APC July 2023 Developed in collaboration with Central London Community Healthcare NHS Trust, West Herts Hospital NHS Trust, East and north Herts hospital NHS Trust, Hertfordshire community Trust and Hertfordshire CCG's