Hertfordshire and West Essex adult (age≥18 years) treatment pathway
SGLT2 inhibitors for treating chronic heart failure.

Initiation criteria in line with NICE TA 679, 773, 902 and 929
Dapagliflozin and Empagliflozin are recommended as an option for treating symptomatic chronic heart failure in adults with:

Reduced ejection fraction (HFrEF):
- LVEF ≤ 40%
- NYHA II –IV
- Only to be used as an add on to optimised standard care with
  - ACE inhibitor / ARB or sacubitril/valsartan and
  - Beta blocker and
  - Mineralocorticoid receptor antagonist (MRAs) if tolerated

Mildly reduced ejection fraction (HFmrEF)
- LVEF 40-49%
- NYHA II –IV

Preserved ejection fraction (HFpEF)
- LVEF ≥50% with structural heart disease (e.g. left ventricular hypertrophy or left atrial dilatation) and / or diastolic dysfunction

Before initiating SGLT2 inhibitor (dapagliflozin or empagliflozin):
1) A diagnosis of heart failure must be confirmed by a cardiologist/HF specialist, based on raised NT-proBNP levels and specialist assessment including ECHO.
2) No risk factors for developing diabetic ketoacidosis (DKA) (only applicable to diabetic patients).

All types of heart failure

Non-diabetic patients and patients with type 2 diabetes mellitus (T2DM) without insulin:

GREEN -Recommended for initiation in Community, Secondary or Tertiary care. Initiation may also be undertaken in primary care on the recommendation of a heart failure specialist or by primary care health professionals with a specialist interest in heart failure or who have the relevant expertise (for example, undergone relevant training).

NB: existing patients in primary care diagnosed with HFmrEF and HFpEF; SGLT2 inhibitor therapy can be initiated where an ECHO report is available (within 3 years, unless clinical situation has changed). Existing patients where the diagnosis is unclear, seek specialist advice prior to initiation as required.

For patients with T2DM with insulin:

AMBER INITIATION – recommended for restricted use - initiation by heart failure specialist or community/secondary care diabetes specialist teams. Continuation in primary care. Primary care health professionals with specialist interest in diabetes or who have undertaken the relevant training, may initiate.

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

Exclusion criteria

- **Type 1 diabetic mellitus**
- *Renal function*: eGFR <15ml/min for dapagliflozin, eGFR <20ml/min for empagliflozin
- 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 (including for those patients on Total Diet Replacement (TDR)
- 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
- *Severe impaired hepatic function* (*empagliflozin*): not recommended

Cautions for initiation

- *Severe impaired hepatic function* (*dapagliflozin*): 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
- Patients at increased risk of volume depletion (dehydration, hypovolaemia and hypotension): *SGLT2i have a diuretic effect which may lead to dehydration.*
  - Frailty/cognitive impairment. Increased risk of dehydration.
  - Diabetes with HbA1c> 86mmol/mol: increased risk due to osmotic symptoms; refer to diabetologist.
  - Patients on diuretics: increased diuresis; *diuretic dose adjustments may be required*.
- Systolic blood pressure below 95mmHg and symptomatic hypotension. *SGLT2 inhibitors increased diuresis which may lead to a modest decrease in blood pressure*. Caution should be exercised in patients for whom a SGLT2i-induced drop in blood pressure could pose a risk, such as patients on anti-hypertensive therapy with a history of hypotension or elderly patients.

Check drug interactions: See summary of product characteristics or British National Formulary for full details: Dapagliflozin SPC; Dapagliflozin BNF; Empagliflozin SPC; Empagliflozin BNF

NB: patients with 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 (eGFR<45ml/min) 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 metformin, GLP-1 receptor agonists and DPP-4 inhibitors (gliptins)**: low hypoglycaemia risk.
  - **Patients on sulphonylureas, a history of hypoglycaemia or with uncontrolled HbA1c** may require doses of existing glucose lowering therapies to be reduced prior to initiation of SGLT-2 to reduce the risk of hypoglycaemia: if required discuss with specialist in diabetes care (in community or secondary care).
  - Where patients are **on triple therapy,** consider replacing a glucose lowering therapy with dapagliflozin or empagliflozin; discuss with specialist in diabetes care (in community or secondary care)
  - **Patients on insulin**: refer to/discuss with specialist in diabetes care (in community or secondary care)

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).

At initiation, discuss adverse effects and cautions for use including providing the following information to the patient:
- urine volume increase and risk of dehydration. Advice patients at risk of hypotension on signs and symptoms of hypotension.
- sick days, suspend SGLT2 inhibitor if vomiting, severe sepsis and peri-operatively (inform prescriber)
- fungal genital infection, counsel on genital hygiene and advise to stop SGLT2 inhibitor and seek urgent medical help if get symptoms of Fournier's gangrene (rare, MHRA alert)
- avoidance of foot complications - suspend SGLT2 inhibitor if acute foot ulceration/ischaemia (MHRA alert)
- Counsel patients on symptoms of DKA (MHRA alert) and T2DM sick-day rules (temporarily stop if they are unable to eat and drink or are fasting)
- Advise patients to not start a very low carbohydrate diet or ketogenic diet without discussing it with their health professional, because they may need to suspend the SGLT-2 inhibitor treatment.

Suggested 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

Specialists transferring prescribing to primary care: Communicate to the GP clearly noting the indication for SGLT2 inhibitor as heart failure and request addition to repeat prescription.

Ongoing monitoring:
There is no specific requirement for monitoring dapagliflozin and empagliflozin.

- Renal function should be monitored according to current guidelines for heart failure. A modest initial decline in eGFR that is hemodynamic in nature and reversible is characteristic of SGLT2 inhibitors and would generally not be an indication to discontinue therapy.
  NICE CG106 '*Chronic heart failure in adults: diagnosis and management*': The frequency of monitoring should depend on the clinical status and stability of the person. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has changed but is needed at least 6-monthly for stable people with proven heart failure.
- Follow up for diabetic care (T2DM patients only): by the patient usual diabetic care provider. Monitor HbA1c in T2DM patients every 3 to 6 months (tailored to individual needs) until HbA1c is stable on unchanging therapy, then every 6 months as per NICE NG28.

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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Phone 01438 284574, email nurseledheartfailure.enh-tr@nhs.net
West Herts Hospital Trust heart function team
phone 01923 217421, email westherts.heartfunction@nhs.net
Central London Community Healthcare NHS Trust, Heart failure team
Phone 0208 102 5891, email clcht.westherts.communitycardiology@nhs.net
Essex Partnership University NHS Foundation Trust, Community Heart Failure Nurse Specialists
Phone 01279 621925, email epunft.cardiacnurses@nhs.net
The Princess Alexandra Hospital heart failure nurse specialist team
Phone 01279 962247, email tpa-tr.heartfailure.pah@nhs.net
Hertfordshire Community Trust, Integrated heart failure team
Phone 01438 583239, email hct.ihfs@nhs.net

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 download (hweclinicalguidance.nhs.uk)
6. Hertfordshire and West Essex adult (age ≥18 years) treatment pathway Dapagliflozin, Empagliflozin & Canagliflozin for treating Chronic Kidney Disease (CKD) with or without Type 2 Diabetes based on NICE TA775, NICE TA 942, NICE NG28 and NG203, accessed via download (hweclinicalguidance.nhs.uk)

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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