Dapagliflozin▼ and empagliflozin▼ in Heart Failure with Reduced Ejection Fraction (HFrEF) in patients with and without Diabetes Mellitus: Sheffield guidance for primary care

Dapagliflozin and empagliflozin are recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction in adults, only if used as an add-on to optimised standard care[1,4]:

- They are already on optimal therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), OR
- They are already on optimal therapy with sacubitril valsartan#, beta blocker and, if tolerated, an MRA.

Sacubitril valsartan is an angiotensin receptor neprilysin inhibitor (ARNI)

Dapagliflozin and empagliflozin (SGLT2 inhibitors) are **Amber** on the Sheffield Traffic light drug list for use in HFrEF; the pathway in Sheffield for initiation and monitoring differs in diabetic and non-diabetic patients, as indicated below.

NON-Diabetic patients

Initiation

Specialist (cardiologist or heart failure specialist nurse) to initiate, counsel and prescribe the initial supply.

Type 2 Diabetic patients ONLY

Initiation

Specialist (cardiologist or heart failure specialist nurse) to initiate, counsel and prescribe initial supply, unless the patient is on **insulin and/or sulfonylurea.** In this case, primary care clinician will be asked by the specialist to prescribe dapagliflozin/empagliflozin with the support of the community diabetes specialist nurse (DSN)* to titrate doses of insulin/diabetic medication in line with glucose control.
*Primary care clinician to refer to DSN

Dapagliflozin 10mg OD - no titration (5mg dose initially in severe hepatic disease)
Empagliflozin 10mg OD- no titration
Highlight in clinical record the indication for dapagliflozin or empagliflozin as heart failure (**HFrEF**) to ensure it is not stopped in diabetic patients at routine diabetes review.

Dapagliflozin should **only** be initiated for HFrEF if: [2,3,6]

- Systolic blood pressure is **>95 mmHg** and
- **eGFR is ≥30 ml/min/1.73m²**
  Note: local recommendation, differs from SPC

Empagliflozin should **only** be initiated for HFrEF if: [4,5,6]

- Systolic blood pressure is **>95 mmHg** and
- **eGFR ≥ 20ml/min/1.73m²**

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Monitoring for Type 2 diabetics & non-diabetics[3,6]

Secondary care: Baseline U&Es
Primary care: thereafter **3 monthly** U&Es, BP, Weight (& HbA1C in diabetic patients only)
(note: U&E monitoring is already for purpose of existing medication regimen including either ACEI/ARB and MRA **or** ARNI and an MRA)
OR
6 Monthly U&Es, BP & weight if the SGLT2 inhibitor is added to one of the above drugs used alone.

Renal Impairment[2,3,4,6]

- Dapagliflozin and empagliflozin are **licensed** for use in HFrEF with reduced eGFR.
- A drop in eGFR is expected within 1 month of initiation; the initial decline stabilises after 3 months.
- Deterioration below the eGFR above will usually require either a discussion with the heart failure specialists (cardiologist or nurses), or a referral to the renal physician who will advise accordingly.
- In patients treated with dapagliflozin/empagliflozin for HFrEF and type 2 diabetes mellitus, additional glucose-lowering treatment may need to be considered if eGFR falls persistently **below 45ml/min/1.73m^2** (as SGLT2 inhibitors have minimal effect on glycaemic control with reduced renal function).

Patient counselling & advice for ALL patients[6]

Counsel patient about the risks of hypotension, and the increased incidence of genito-urinary candidiasis and the rare occurrence of Fournier's gangrene.
If they become ill for any reason and are unable to maintain an adequate fluid intake or become dehydrated, to avoid the risk of ketoacidosis, dapaglifozin/empagliflozin should be **discontinued** and restarted when the patient is eating and drinking normally again.

Additional patient counselling & advice for DIABETIC patients ONLY

Inform patients with **diabetes** of the signs and symptoms of diabetic ketoacidosis (DKA) and advise them to seek immediate medical advice if they develop any of these.
There is a small risk of hypoglycaemia which will be mitigated against through adjustments to their other diabetes medication (particularly in those who are on more than one hypoglycaemic agent).

Caution- Patients can present with euglycaemic DKA when treated with SGLT2 inhibitors – see MHRA safety alert

Forxiga® (dapagliflozin) in HFrEF patient information booklet available here
Jardiance ® (empagliflozin) in HFrEF patient information booklet available here
STH patient information booklet for dapagliflozin in patients with HFrEF is here
Clinical Knowledge Summaries for SGLT2 inhibitors in HFrEF is here

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References

1. National Institute for Health and Care Excellence. NICE TA679: Dapagliflozin for treating chronic heart failure with reduced ejection fraction Feb 2021 https://www.nice.org.uk/guidance/ta679/chapter/1-Recommendations

2. Astra Zeneca UK Ltd. Summary of Product Characteristics; Forxiga 10mg film-coated tablets, accessed 13th December 2021 https://www.medicines.org.uk/emc/product/7607/smpc

3. STH Prescribing Guideline: Prescribing guideline: Dapagliflozin and empagliflozin for the treatment of chronic heart failure with reduced ejection fraction (HFrEF) (non-diabetics) (April 2023) and personal communication Dr Ahmed Iqbal Honorary Consultant Physician/Diabetes (Dec 2021)

4. National Institute for Health and Care Excellence. NICE TA773 : Empagliflozin for treating chronic heart failure with reduced ejection fraction. March 2022. https://www.nice.org.uk/guidance/ta773/chapter/1-Recommendations

5. Boehringer Ingelheim Limited. Summary of Product Characteristics; Jardiance 10mg film-coated tablets ,4th November 2022 https://www.medicines.org.uk/emc/product/5441/smpc

6. STH Prescribing Guideline: Sodium Glucose Co-Transporter 2 Inhibitors (SGLT2i), Combined Cardio-Renal-Metabolic Prescribing Guideline for use in adult patients with and without diabetes. Dr Ahmed Iqbal, Dr Arif Khwaja, Prof Abdallah Al Mohammad (April 2022)

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This guideline has been adapted to include empagliflozin from the 'Dapagliflozin▼ in Heart Failure with Reduced Ejection Fraction (HFrEF) in patients with and without Diabetes Mellitus: guidance for primary care' approved by APG Jan 2022

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