

## Use of Dapagliflozin & Empagliflozin (SGLT2i) in Patients with Heart Failure

Dapagliflozin and Empagliflozin are now indicated for use in patients with heart failure

### • Indications:

- Symptomatic chronic heart failure NYHA 2-4 and either:
  - Reduced ejection fraction (EF<50%) as per [NICE TA679](#) and [NICE TA773](#) as an 'add-on' therapy to optimised standard care with ACEi/ARB/ARNI,  $\beta$ -blockers & mineralocorticoid receptor antagonists (MRAs).
  - Preserved or mildly reduced ejection fraction (EF>50%) as per [NICE TA902](#) and [NICE TA929](#) as an option for treating symptomatic chronic heart failure with preserved or mildly reduced ejection fraction

### • Contraindications:

- Type 1 diabetes mellitus
- History of DKA
- Hypersensitivity to SGLT2i
- Pregnancy / breast-feeding

Dapagliflozin and Empagliflozin for the treatment of heart failure have an AMBER specialist recommended traffic light status on BNSSG formulary. These medicines are suitable for GP prescribing following specialist **recommendation**.

***This means either the GP or specialist can provide the first prescription***

### General Considerations for use of Dapagliflozin or Empagliflozin

- Ensure HbA1c has been checked
- Clearly document the indication for use of SGLT2i.

### Dapagliflozin

- The recommended dose of dapagliflozin for heart failure is 10mg once daily.
- Adjust to 5mg daily in severe hepatic impairment (Child Pugh Class C).
- Therapy to be taken at any time of day, with or without food. To be swallowed whole.

### Empagliflozin

- The recommended dose of empagliflozin for heart failure is 10 mg once daily.
- No dose adjustment is required for patients with hepatic impairment. Not recommended in patients with severe hepatic impairment.
- The tablets can be taken with or without food, swallowed whole with water.

## Sequencing of Heart Failure Therapy

- For reduced ejection fraction, large-scale studies support the **combined** use of ACEi/ARB/ARNI,  $\beta$ -blockers, MRAs and SGLT2i in heart failure with reduced ejection fraction.
- Each drug group has been shown to reduce morbidity & mortality within 30 days so aim to establish all 4 groups.
- For preserved ejection fraction, clinical trials show that dapagliflozin/empagliflozin + plus standard care reduces the combined risk of death from cardiovascular causes or likelihood of first hospitalization for heart failure

## Use of Dapagliflozin or Empagliflozin for Heart Failure in Renal Impairment

- After initiation of dapagliflozin or empagliflozin, renal function usually declines but resolves within 1-3 months. No specific renal monitoring required see [Traffic Lights: How to monitor renal function and potassium rises in stable heart failure](#)

### Dapagliflozin

- Can initiate in patients with eGFR  $\geq$  15ml/min/1.73m<sup>2</sup>
- If eGFR drops  $<$  15ml/min/1.73m<sup>2</sup> during treatment whilst on dapagliflozin, **do not stop** treatment without discussion with heart failure or renal specialist (A&G route for NBT renal consultant opinion )

### Empagliflozin

- Can initiate in patients with eGFR  $\geq$  20 ml/min/1.73m<sup>2</sup>
- $<$  20 ml/min/1.73m<sup>2</sup> not recommended

## Use of SGLT2i's in diabetic patients with Heart Failure

- In primary care, practice nurse & clinical pharmacist services should be utilized
- When used in Type 2 DM, the glucose lowering effects of SGLT2i's are less effective when eGFR  $<$ 45ml/min/1.73m<sup>2</sup> and additional glucose-lowering medication may be needed. Therefore, cut-off for use is for lack of efficacy for glucose-lowering, not safety for continuing for HF or CKD indications.
- **Consider referral to secondary care** if people have complex diabetes, CKD stage 3, not achieving treatment targets despite support from primary care & specialist community DM teams.
- Some patients will need specialist diabetes advice when considering initiating therapy ; see table below.

Current Treatment	Refer to:	Comments
Diet, lifestyle & behavioural management	HF team to initiate SGLT2i	Low risk of hypoglycaemia. Counsel patient re: risk of DKA.
Metformin, GLP1A (glutide) or DDP4i (gliptin)therapy	HF team to initiate SGLT2i	Low risk of hypoglycaemia. Counsel patient re: risk of DKA.
Sulphonylureas e.g. gliclazide	HF team to initiate SGLT2i  If HbA1c $<$ 58 mmol/mol consider discussing with specialist looking after their DM or use Sirona A&G line.	Risk of hypoglycaemia. Counsel patient re: risk of DKA & hypos.
Insulin	HF team to initiate SGLT2i.  If HbA1c $<$ 58 mmol/mol consider discussing with specialist looking after their DM or use Sirona A&G line.	Risk of hypoglycaemia. Counsel patient re: risk of DKA, hypos & need to titrate insulin. Consider secondary care referral as above.

## Special Circumstances for Use of SGLT2i

- Acute intercurrent illness/volume depletion and peri-operative use (major surgical procedures only); stop treatment. Restart once patient eating & drinking normally [BNSSG Sick Day Rules](#)
- As SGLT2i have a mild diuretic effect, a review of concurrent diuretics may be required when initiating therapy (eg reduce loop diuretic dose).
- Systolic BP < 95mmHg; usually SGLT2i can be safely started but caution if patient has postural symptoms **before** starting therapy.
- Euglycaemic DKA is a very rare complication of SGLT2i, almost always occurring in people with T2DM; however it can occur in non-diabetics after severe restriction of carbohydrate intake. Withhold therapy if clinically suspected, irrespective of blood glucose

## Adverse Reactions with SGLT2i

Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Very rare (<1/10,000)
<b>Hypoglycaemia</b>	<b>Genital Infections and UTI</b>	<i>Constipation</i>	<b>Euglycaemic DKA</b>	<i>Fournier's gangrene</i>
<u>Volume Depletion</u>	<i>Dizziness</i>	<i>Dry mouth</i>	<u>Fournier's gangrene</u>	<i>Angioedema</i>
	<i>Skin Rashes</i>	<i>Nocturia</i>		
	<i>Back Pain</i>	<i>Fungal infections</i>		
	<i>Dysuria / Polyuria</i>	<i>Volume Depletion</i>		
	<u>Thirst</u>	<i>Thirst</i>		
	<u>Constipation</u>	<i>Vulvovaginal pruritis</i> <i>Genital pruritis</i>		
	<u>Pruritis (generalised)</u>	<u>Urticaria</u>		
	<u>Rash</u>	<u>Angioedema</u>		
	<u>Increased urination</u>	<u>Dysuria</u>		

■ **Dapagliflozin and Empagliflozin**

■ *Dapagliflozin*

■ Empagliflozin

## Patient Advice

These documents can be used to counsel patients on the safety precautions for these treatments:

- [Forxiga-Heart-failure-Patient-Booklet-Updated](#)
- [Empagliflozin Patient Information Leaflet](#)
- [TREND](#) leaflet which includes SGLT2s
- [BNSSG Sick Day Rules Guidance](#)

## Further Reading & References

- <https://www.nice.org.uk/guidance/ta679> (Dapagliflozin)
- <https://www.nice.org.uk/guidance/ta773> (Empagliflozin)
- [Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction - NEJM](#)
- [Cardiovascular and Renal Outcomes with Empagliflozin in HF - NEJM](#)
- [Dapagliflozin in Chronic Kidney Disease – NEJM](#)
- [Dapagliflozin SPC](#)
- [Empagliflozin SPC](#)

## Contact Details

For further advice on use of dapagliflozin or empagliflozin in heart failure with reduced ejection fraction, please contact;

- **NBT:** Dr C Wong. Dr A Power
- **UHBW (BRI site):** Dr Y Ismail. Dr A Nightingale. Dr Rami Fikri
- **UHBW (WGH site):** Dr G Dalton
- **Sirona:** Nicki Mead