Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

NICE Technology Appraisals: Local implementation

NICE TA Guidance	**Empagliflozin for Treating Chronic Heart Failure with Reduced Ejection Fraction (NICE TA773)**		
Available at	https://www.nice.org.uk/guidance/ta773		
Date of issue	09 March 2022	**Implementation deadline**	09 June 2022

Medicine details	
Name, brand name	Empagliflozin (Jardiance®)
Manufacturer	Boehringer Ingelheim Limited
Licensed indication	**Therapeutic indications** [SPC accessed 15/04/22 17:25] Heart failure Empagliflozin is indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.
Formulation	**Pharmaceutical form** [SPC accessed 15/04/22 17:25] Empagliflozin 10 mg film-coated tablets Round, pale yellow, biconvex, bevel-edged film-coated tablet debossed with “S10” on one side and the Boehringer Ingelheim logo on the other (tablet diameter: 9.1 mm).
Usual dosage	**Posology** [SPC accessed 15/04/22 17:25] Heart failure The recommended dose is 10 mg empagliflozin once daily.
NICE, recommended dosage/schedule	As per marketing authorisation above.

Disease and potential patient group

Brief description of disease	Heart failure means that the heart is unable to pump blood around the body properly. It usually occurs because the heart has become too weak or stiff. It can occur at any age but is most common in older people. Heart failure is a long-term condition that tends to get gradually worse over time. It can severely limit the activities you are able to do and is often eventually fatal. The main symptoms of heart failure are breathlessness after activity or at rest, feeling tired most of the time and swollen ankles & legs. Treatment for heart failure (depending on the cause) usually aims to control the symptoms for as long as possible and slow down the progression of the condition. Conditions that can lead to heart failure include coronary heart disease, high blood pressure, cardiomyopathy, arrythmias such as atrial fibrillation, heart valves problems and congenital heart disease. Sometimes anaemia, drinking too much alcohol, an overactive thyroid or high pressure in the lungs (pulmonary hypertension) can also lead to heart failure. https://www.nhs.uk/conditions/heart-failure/ [accessed 15/04/22 18:54] Heart failure is divided into types depending on how much blood the heart manages to pump out in each heartbeat. If less than 40% of the blood is pumped out, this is called heart failure with reduced ejection fraction (HFrEF). If more than 40% is pumped out, it is called heart failure with preserved ejection fraction. Distinguishing between the two is important as it will affect the treatment which is used. Approximately 50% of patients with heart failure are classed as having HFrEF https://patient.info/heart-health/heart-failure-leaflet [accessed 29/04/2022 15:55] Heart failure affects around 900,000 people in the UK, and this number is likely to rise, due to an ageing population, more effective treatments, and improved survival rates after a heart attack. Heart failure is a large burden on the NHS, accounting for 1 million bed days per year, 2% of the NHS total, and 5% of all emergency admissions to hospital. National Cardiac Audit Programme [accessed 29/04/2022 15:55] About 50% of people with heart failure die within 5 years of diagnosis, and about 40% of people admitted to hospital with heart failure die or are readmitted within 1 year. NICE CKS Heart Failure [accessed 29/04/2022 15:55] **Heart failure with reduced ejection fraction is associated with high rates of cardiovascular death and hospitalisation**
Potential patient numbers per 100,000	**Table 1 Number of People eligible for treatment in Surrey Heartlands** Source NICE TA773 resource impact template. https://www.nice.org.uk/guidance/ta773 [accessed 21/04/22 17:41]

People eligible for treatment		Local assumption current practice % of people at year 5	Local assumption current practice number of people at year 5	Local assumption future practice % of people at year 5	Local assumption future practice number of people at year 5
Total population for area selected (all ages)			1,049,170		1,049,170
Population of England 18 years or older		-	815,884	-	815,884
People with heart failure on quality and outcomes framework (QOF)		0.90%	7,343	0.90%	7,343
People with symptomatic chronic heart failure on QOF with a confirmed diagnosis		80.14%	5,885	80.14%	5,885
People with symptomatic chronic heart failure with left ventricular systolic dysfunction (heart failure with reduced ejection fraction: HFrEF)		50.25%	2,957	50.25%	2,957
People with symptomatic chronic HFrEF symptomatic with New York Heart Association (NYHA) classification II to IV		90.90%	2,688	90.90%	2,688
People with symptomatic chronic HFrEF with eGFR >30 mL/min per 1.73 m2		79.79%	2,145	79.79%	2,145
People with symptomatic chronic HFrEF receiving optimised standard care based on ACE inhibitors or ARBs, or based on sacubitril valsartan		83.00%	1,780	83.00%	1,780
People whose symptoms continue despite receiving optimised standard of care, or based on sacubitril valsartan		78.00%	1,389	78.00%	1,389
Total		**100%**	**1,389**	**100%**	**1,389**
Treatments: Full year					
People receiving optimised standard care based on ACE inhibitors or ARBs		20%	278	20%	278
People receiving optimised standard care based on sacubitril valsartan		5%	69	5%	69
People receiving dapagliflozin add-on to standard care based on sacubitril valsartan		25%	347	13%	174
People receiving dapagliflozin add-on to standard care based on ACE inhibitors or ARBs		50%	694	25%	347
People receiving empagliflozin add-on to standard care based on sacubitril valsartan		0%	0	13%	174
People receiving empagliflozin add-on to standard care based on ACE inhibitors or ARBs		0%	0	25%	347
Total		**100%**	**1,389**	**100%**	**1,389**

Figures assume that either Empagliflozin or Dapagliflozin (TA679) could be used for the same patient cohort.

Figures assume equal market share between Empagliflozin and Dapagliflozin at year 5.

Potential patient numbers receiving Empagliflozin at year 5 => 174+347 = 521 (assuming 50% market share with Dapagliflozin)

Total number of people potentially eligible for treatment with an SGLT2i (Empagliflozin or Dapagliflozin) for symptomatic HFrEF in Surrey Heartlands at year 5 = 1389
This equates to potential patient numbers per 100,000 of 139

SUMMARY

NICE recommendation

1 Recommendations

1.1 Empagliflozin is 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:

- an angiotensin-converting enzyme (ACE) inhibitor or angiotensin 2 receptor blocker (ARB), with a beta blocker and, if tolerated, a mineralocorticoid receptor antagonist (MRA), or
- sacubitril valsartan with a beta blocker and, if tolerated, an MRA.

1.2 Start empagliflozin for treating symptomatic heart failure with reduced ejection fraction on the advice of a heart failure specialist. Monitoring should be done by the most appropriate healthcare professional.

1.3 This recommendation is not intended to affect treatment with empagliflozin that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue

without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

People with heart failure with reduced ejection fraction may have symptoms that are not controlled well enough despite being on the most appropriate (optimised) standard care. Standard care includes an ACE inhibitor or an ARB, with a beta blocker and, if tolerated, an MRA. Then, if symptoms continue on this, people may be offered sacubitril valsartan with a beta blocker and, if tolerated, an MRA.

Evidence from a clinical trial show that empagliflozin plus standard care reduces the risk of dying from cardiovascular causes compared with placebo plus standard care. It also shows that it reduces the likelihood of hospitalisation for heart failure. There are no trials directly comparing empagliflozin with the most appropriate comparator, dapagliflozin. However, an indirect comparison suggests that empagliflozin is likely to be similar to dapagliflozin in reducing the risk of dying and the likelihood of hospitalisations for heart failure.

The cost-effectiveness estimates for empagliflozin are within what NICE normally considers an acceptable use of NHS resources. So empagliflozin is recommended.

Increased monitoring or changes to other medicines being taken may be needed for treating heart failure with empagliflozin. So, it should only be started on advice from a heart failure specialist.

Cost implications*

Cost of product:

The list price of 10 mg Empagliflozin (Jardiance®) is
£36.59 (plus VAT) per 28 days [Drug tariff April 2022 accessed 16/04/22]

Of note alternative SGLT2i licensed for symptomatic HFrEF:
The list price of 10 mg Dapagliflozin (Forxiga®) is
£36.59 (plus VAT) per 28 days [Drug tariff April 2022 accessed 16/04/22]

Annual cost per patient: £36.59/28 x 365 days = £476.98 (plus VAT)

Has dose escalation been considered as part of the NICE costing template?
No dose escalation specified in the SPC for the indication of Heart Failure. [SPC accessed 15/04/22 17:25]

Costing information for Surrey Heartlands

We do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £9,000 per 100,000 population, based on a population for England of 56.3 million people).
This is because the technology is a further treatment option, and the overall cost of treatment will be similar.
NICE TA773 Resource Impact Statement https://www.nice.org.uk/guidance/ta773

Table 2 Costing information for Surrey Heartlands CCG

Treatment of chronic heart failure with reduced ejection fraction (TA679 Dapagliflozin & TA773 Empagliflozin)

Resource impact template

NICE National Institute for Health and Care Excellence

Drug costs	Unit Cost	Activity current practice at year 5	Activity future practice at year 5	Activity change at year 5	Cost of current practice at year 5	Cost of future practice at year 5	Impact of change on cost at year 5
People receiving optimised standard care based on ACE inhibitors or ARBs	£44	278	278	0	£12,089	£12,089	£0
People receiving optimised standard care based on sacubitril valsartan	£1,237	64	64	0	£79,362	£79,362	£0
People receiving dapagliflozin add-on to standard care based on sacubitril valsartan	£1,714	321	160	-160	£549,805	£274,902	-£274,902
People receiving dapagliflozin add-on to standard care based on ACE inhibitors or ARBs	£521	646	323	-323	£336,086	£168,043	-£168,043
People receiving empagliflozin add-on to standard care based on sacubitril valsartan	£1,714	0	160	160	£0	£274,902	£274,902
People receiving empagliflozin add-on to standard care based on ACE inhibitors or ARBs	£521	0	323	323	£0	£168,043	£168,043
People receiving optimised standard care based on sacubitril valsartan and discontinuing in year	£640	5	5	0	£3,379	£3,379	£0
People receiving dapagliflozin add-on to optimised standard care based on sacubitril valsartan and discontinuing in year	£879	26	13	-13	£23,185	£11,593	-£11,593
People receiving dapagliflozin add-on to optimised standard care based on ACE inhibitors or ARBs and discontinuing in year	£282	49	24	-24	£13,706	£6,853	-£6,853
People receiving empagliflozin add-on to optimised standard care based on sacubitril valsartan and discontinuing in year	£879	0	13	13	£0	£11,593	£11,593
People receiving empagliflozin add-on to optimised standard care based on ACE inhibitors or ARBs and discontinuing in year	£282	0	24	24	£0	£6,853	£6,853
Total drug costs		**1,389**	**1,389**	**0**	**£1,017,610**	**£1,017,610**	**£0**

The unit price drug, dosing frequency and method of administration of Empagliflozin 10mg and Dapagliflozin 10mg are equivalent for patients with symptomatic heart failure with reduced ejection fraction and NICE predicts a 50:50 market share between Empagliflozin and Dapagliflozin for this patient cohort.

The committee (NICE TA733) was satisfied that empagliflozin is similarly effective to dapagliflozin and that its costs are identical. For the assumption of equal effectiveness, the results showed no difference in total costs or quality-adjusted life years between the 2 treatments. The committee was satisfied that empagliflozin is similarly effective to dapagliflozin and that its costs are identical. https://www.nice.org.uk/guidance/ta773/chapter/3-Committee-discussion#cost-effectiveness-estimates (accessed 15/04/22)

Dapagliflozin for treating chronic heart failure with reduced ejection fraction TA679 was implemented by Surrey Heartlands in May 2021.

Empagliflozin offers an alternative SGLT2i option to Dapagliflozin for people with symptomatic HFrEF

The impact of change on total drug cost at year 5 is zero (see table 2).

Table 2a. Costing information for Surrey Heartlands CCG cont'd

The use of Empagliflozin (or Dapagliflozin) may help reduce hospitalisation associated with heart failure and could save on average £2845 per episode.

Treatment of chronic heart failure with reduced ejection fraction (TA679 Dapagliflozin & TA773 Empagliflozin)							
Resource impact template					NICE National Institute for Health and Care Excellence		
Drug costs	Unit Cost	Activity current practice at year 5	Activity future practice at year 5	Activity change at year 5	Cost of current practice at year 5	Cost of future practice at year 5	Impact of change on cost at year 5
Savings from reduced hospitalisations of people treated with dapagliflozin or empagliflozin							
Hospitalisations with standard care based on ACE inhibitors or ARBs		54	54	0			
Hospitalisations with standard care based on sacubitril valsartan		13	13	0			
Hospitalisation with dapagliflozin add-on treatment to standard care based on sacubitril valsartan		42	21	-21			
Hospitalisations with dapagliflozin add-on treatment to standard care based on ACE inhibitors or ARBs		84	42	-42			
Hospitalisation with empagliflozin add-on treatment to standard care based on sacubitril valsartan		0	23	23			
Hospitalisations with empagliflozin add-on treatment to standard care based on ACE inhibitors or ARBs		0	46	46			
Savings from reduced hospitalisations of people treated	£2,845	**193**	**200**	**7**	**£547,979**	**£567,827**	**£19,848**
Resource impact					**£1,565,590**	**£1,585,438**	**£19,848**

Surrey Heartlands will experience a cost pressure of approximately £20,000 over the next 5 years. The figure does not exceed the £100,000 cost pressure threshold for each of the four places (East Surrey, Guildford & Waverley, Northwest Surrey, Surrey Downs)

Availability of PAS and details (if appropriate): NO

Availability of homecare service (if appropriate): NO

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

Current Treatment pathway and proposed place in therapy

Please see Appendix 1
Treatment pathway for HFrEF based on NICE NG106 Chronic heart failure in adults and proposed place in therapy of Empagliflozin**.** Pathway adapted from SWL Heart Failure pharmacological guidelines July 2020- adopted by Surrey Downs https://surreyccg.res-systems.net/PAD/Guidelines/Detail/6202

NOTE: NICE TA775 Dapagliflozin for treating chronic kidney disease (CKD) was published March 2022. When NICE TA775 is implemented in Surrey Heartlands, it is anticipated that patients with symptomatic chronic HFrEF and CKD could be preferentially initiated on Dapagliflozin rather than Empagliflozin (which does not currently have a license for CKD).

Impact to patients

- Alternative oral treatment option (to Dapagliflozin) for symptomatic heart failure with reduced ejection fraction when added on to optimised standard care.
- Empagliflozin has shown a reduction in hospital admissions for HFrEF and a slower progressive decline in renal function regardless of the presence or absence of diabetes. Patients taking Empagliflozin are likely to have fewer hospitalisations for HFrEF and have a more favourable renal function (from 76 weeks on treatment) compared with placebo
- No licensed liquid formulation available. Tablets to be swallowed whole with water. May impact on patients with swallowing difficulties.
- No special storage required.
- No dose adjustment based on age is required. However, the SPC for Empagliflozin states: In patients 75 years and older, an increased risk for volume depletion should be taken into account. Special attention should be given to their volume intake in case of co-administered medicinal products which may lead to volume depletion (e.g., diuretics, ACE inhibitors). **In patients aged 85 years and older, initiation of empagliflozin therapy is not recommended due to the limited therapeutic experience.**

  Of note, the average age in the intention-to-treat population of the Emperor-Reduced trial (seminal

trial for Empagliflozin plus optimised standard care vs placebo plus optimised standard care to treat patients with symptomatic HFrEF) was 67yrs while the average age in the NHS at diagnosis is 77yrs.

NICE TA773 comment regarding age:

The committee noted EMPEROR-Reduced was not powered to show any difference in subgroups by age. The clinical experts said there would be no apparent reason why relative treatment effects would be different between subgroups of younger and older ages. The committee concluded that data from the intention-to-treat population in EMPEROR-Reduced was broadly generalisable to NHS clinical practice. https://www.nice.org.uk/guidance/ta773/chapter/3-Committee-discussion#the-condition (accessed 22/04/22)

Impact to primary care prescribers

Availability:

Widley available. Currently no supply issues.

Prescribing impact:

If the proposed BLUE traffic light status is assigned to Empagliflozin for HFrEF then there will be no formal shared care agreement in place, but primary care can access advice from the heart failure specialist if required for onward management.

Empagliflozin is prescribed currently in primary care for patients with diabetes. It holds a Green traffic light status for this indication.

Primary care prescribers must clearly document the indication for Empagliflozin (Heart failure) on the patient's medical notes. This is to ensure that Empagliflozin is not stopped at a routine diabetes review.

Monitoring:

The majority of monitoring may fall within primary care as they are commonly performed tests (BP & renal function). NICE TA773 states: Monitoring should be done by the most appropriate healthcare professional.

Monitoring of **renal function** is recommended by the SPC as follows:

- Prior to Empagliflozin initiation and periodically during treatment, i.e., at least yearly
- Prior to initiation of any concomitant medicinal product that may have a negative impact on renal function. [SPC accessed 15/04/22 17:25]

Note: Results from the Emperor-Reduced trial showed that the mean adjusted eGFR fell by 4ml/min/1.73m^2 in the Empagliflozin arm compared to a fall of 1ml/min/1.73m^2 in the placebo group (at 4 weeks post initiation) from baseline. At 12 weeks post initiation, the eGFR recovered by approximately 1.5ml/min/1.73m^2 in the Empagliflozin arm and showed a slower decline compared to placebo over 124 weeks. The risk of the composite renal outcome was lower in the empagliflozin group than in the placebo group. See figure 3.

Figure 3 Changes in eGFR for Empagliflozin and placebo from Emperor-Reduced ;Cardiovascular and renal outcomes with Empagliflozin in Heart Failure

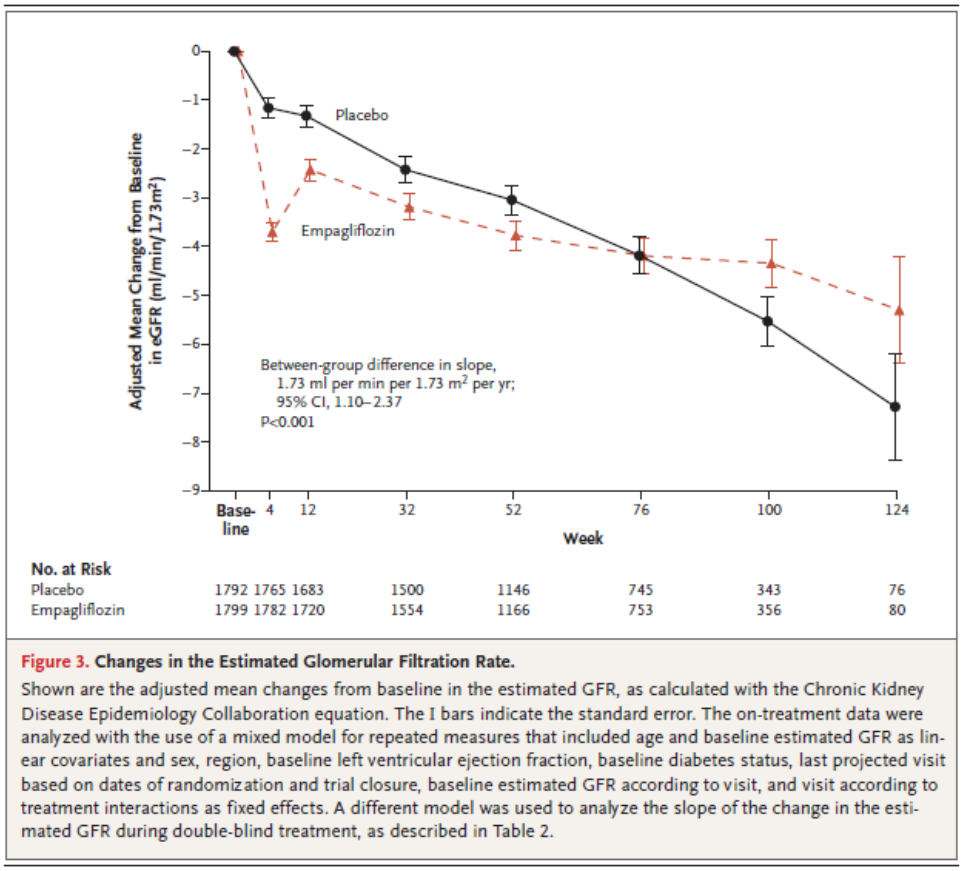

Figure 3. Changes in the Estimated Glomerular Filtration Rate.

Shown are the adjusted mean changes from baseline in the estimated GFR, as calculated with the Chronic Kidney Disease Epidemiology Collaboration equation. The I bars indicate the standard error. The on-treatment data were analyzed with the use of a mixed model for repeated measures that included age and baseline estimated GFR as linear covariates and sex, region, baseline left ventricular ejection fraction, baseline diabetes status, last projected visit based on dates of randomization and trial closure, baseline estimated GFR according to visit, and visit according to treatment interactions as fixed effects. A different model was used to analyze the slope of the change in the estimated GFR during double-blind treatment, as described in Table 2.

Monitoring of **blood pressure** as per SPC:

The SPC does not suggest a specific BP monitoring regimen but does state:

'Based on the mode of action of SGLT-2 inhibitors, osmotic diuresis accompanying glucosuria may lead to a modest decrease in blood pressure. Therefore, caution should be exercised in patients for whom 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.' [SPC accessed 15/04/22 17:25]

Note: Results from the Emperor-Reduced trial showed that there was an average 2.4mmHg (±0.4) drop in systolic blood pressure in the Empagliflozin arm compared to 1.7mmHg (± 0.4) in the placebo group from baseline to 52weeks.

NICE NG106 Chronic heart failure in adults recommendation on monitoring treatment: '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.' (accessed 23/05/22)

Note: The current Blue information sheet for Dapagliflozin treatment for chronic HFrEF states, 'Primary care to re-check renal function and blood pressure 4 weeks after initiation for HFrEF.
Blue information sheet Dapagliflozin; Heart failure with reduced ejection fraction NICE TA679 https://surreyccg.res-systems.net/PAD/Search/DrugConditionProfile/6416 (accessed 01/05/22)

Impact to secondary care

- Possible initiation by heart failure specialist (as per Blue information sheet for Dapagliflozin; Heart failure with reduced ejection fraction NICE TA679 https://surreyccg.res-systems.net/PAD/Search/DrugConditionProfile/6416 (accessed 0105/22)) the majority of whom are in secondary care.
- Note NICE TA773 states: Start empagliflozin for treating symptomatic heart failure with reduced ejection fraction on the **advice of a heart failure specialist**.

- As this is not a new add-on therapy but an alternative option to the pre-existing SGLT2 inhibitor (Dapagliflozin), it is anticipated that Empagliflozin will not create any significant additional demand on capacity for clinical teams in its initiation for symptomatic HFrEF patients.
- The discharge/out-patient information must unambiguously state the indication for Empagliflozin i.e., heart failure.
- It is anticipated that the use of Empagliflozin will lead to a reduction in hospital admissions for HFrEF and so reduce the impact on secondary care.

Impact to CCGs

- ICS/CCG are required to comply with the recommendations in a NICE TA within 3 months of its date of publication. For NICE TA773 this needs to be by 9th June 2022.

- Low potential increase in costs in appointments for initiation for patients with heart failure as Empagliflozin is an alternative option to the pre-existing SGLT2 inhibitor (Dapagliflozin).
- Empagliflozin through achieving improved symptom control is likely to reduce primary care appointments (longer term) and reduce hospital admissions for HFrEF
- The resource impact template assumes a 50:50 market share for Empagliflozin vs Dapagliflozin due to the similarity in clinical and cost effectiveness and does not expect the cost pressure threshold of £100,000 to be breached.

Implementation

NICE technology appraisal (TA) 773 recommends Empagliflozin (Jardiance®) as an option for treating symptomatic chronic heart failure with reduced ejection fraction (HFrEF) in adults (≤40%), only if it is used as an add-on to optimised standard care with:

a) angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), **or**

b) sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

Initiation on the advice of a heart failure specialist with monitoring done by the most appropriate healthcare professional.

2.Proposed: Initiation by a heart failure specialist or *on the advice of a heart failure specialist* with transfer to primary care for ongoing prescribing and monitoring without the need for a formal shared care agreement

- Baseline monitoring to be undertaken by the initiator
- Post initiation monitoring based on the clinical decision of the initiator for that patient.
- Ongoing monitoring in primary care to be in line with the SPC for Empagliflozin and NICE guideline NG106
- More frequent monitoring to be considered in frailty, hypotension, volume depletion (see sick day rules below) and initiation of concomitant medicines that may reduce renal function.

If primary care initiate *on advice of a heart failure specialist*, then the advice should include details of the post initiation monitoring requirements for that patient and any actions to be taken based on the results of the monitoring.

3.In patients with HFrEF **and type 2 diabetes** refer for specialist diabetes advice prior to initiation if the patient is taking insulin, has history of previous/frequent hypoglycaemia or if any advice is needed on diabetes management or suitability of an SGLT2i. Diabetic patients should be made aware of the risks of diabetic ketoacidosis (DKA) when taking an SGLT2i, advised not to undertake ketogenic diets and if DKA develops, Empagliflozin should be discontinued immediately.

4.Empagliflozin (Jardiance®) should not be used for treatment of patients with type 1 diabetes. Data from a clinical trial program in patients with type 1 diabetes showed increased ketoacidosis occurrence with common frequency in patients treated with empagliflozin 10 mg and 25 mg as an adjunct to insulin compared to placebo. [SPC accessed 15/04/22 17:25]

5. Renal impairment:

- In patients with HF and without type 2 diabetes - Empagliflozin 10mg daily can be used when eGFR ≥ 20ml/min.

- In patients with both HF and type 2 diabetes – Empagliflozin 10mg daily can be used when eGFR ≥ 20ml/min but because the glycaemic efficacy of Empagliflozin is dependent on renal function, the addition of other anti-hyperglycaemic agents (if required) should be considered if eGFR < 30ml/min.

- In patients with Type 2 Diabetes and no Heart Failure, Empagliflozin should not be initiated in patients with a GFR < 30 mL/min.

- Empagliflozin should not be used in patients with ESRD (end stage renal disease) or in patients on dialysis. There are insufficient data to support use in these patients.

6. Volume depletion and sick day rules:

- In the case of intercurrent conditions such as gastrointestinal illness which can lead to volume depletion, sick day rules should apply and Empagliflozin stopped until the volume depletion is corrected. The following information could be included in an information sheet for prescribers: https://www.dudleyformulary.nhs.uk/download/560/medicines-and-dehydration-briefing-for-professionals-on-the-medicine-sick-day-rules-card

- Elderly: The effect of empagliflozin on urinary glucose excretion is associated with osmotic diuresis, which could affect the hydration status. Patients aged 75 years and older may be at an increased risk of volume depletion. A higher number of these patients treated with empagliflozin had adverse reactions related to volume depletion as compared to placebo (see section 4.8). Therefore, special attention should be given to their volume intake in case of co-administered medicinal products which may lead to volume depletion (e.g., diuretics, ACE inhibitors). [SPC accessed 01/05/22]

7. **Barriers to implementation locally**:

The current BLUE information sheet for Dapagliflozin; Heart failure with reduced ejection fraction NICE TA679 https://surreyccg.res-systems.net/PAD/Search/DrugConditionProfile/6416 (accessed 01/05/22) will require review in order to:

1. Decide whether initiation can be 'on the advice of the heart failure specialist' as per both NICE TA773/TA679 as well as *by* the heart failure specialist as per the current BLUE information sheet for Dapagliflozin.
2. Decide whether the current Dapagliflozin Blue information sheet's requirement for a minimum one month's supply to be prescribed by the initiating heart failure specialist allows enough time for review and stabilisation of the patient (by the heart failure specialist) before transfer to primary care for ongoing prescribing.

3. Decide whether post initiation BP and renal function monitoring should be done:

a) At 4 weeks by the GP as per the Blue Dapagliflozin information sheet or
b) Based on the clinical decision of the initiator for that patient and as a minimum in line with the SPC for Empagliflozin/Dapagliflozin and NICE guideline NG106

4. Update to a generic BLUE information sheet for SGLT2is (Dapagliflozin & Empagliflozin) licensed for use in HFrEF

Recommendation to APC

PbRe: NO


Colour classification guidelines

Recommended traffic light status (see attached guidelines):
BLUE

Additional comments: Empagliflozin 10mg or 25mg is also licensed for the treatment of Type 2 diabetes mellitus.

References:

1. NICE TA733 Empagliflozin in Chronic Heart Failure with Reduced Ejection Fraction https://www.nice.org.uk/guidance/ta773 [accessed 15/04/22]
2. Summary of Product Characteristics (SPC) Jardiance 10mg film coated tablets https://www.medicines.org.uk/emc/product/5441 [accessed 15/04/22]
3. Drug tariff online https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff [accessed 16/04/22]
4. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. M.Packer et al October 2020 Emperor-Reduced (accessed 23/05/22)

Prepared by:

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Declaration of Interest:

None

Date: 01/05/22

Reviewed by:

1. Dr Steve Cookson, Consultant Cardiologist, Clinical Lead Outpatients Transformation, Royal Surrey NHS Foundation Trust, Chair - Area Prescribing Committee, Clinical Lead for Cardiovascular Disease
2. Clare Thomson, Lead Clinical Pharmacist, Leatherhead Primary Care Network.

Declaration of Interest:

XXXX

Date: XXXX