



**North East London**  
**Barts Health NHS Trust**  
**Homerton Healthcare NHS Foundation Trust**  
**Barking, Havering and Redbridge University Hospitals NHS Trust**

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INDIVIDUALISATION OF PATIENT HbA1c TARGETS	<a href="#"><u>2</u></a>
PATIENT DECISION AID FOR CHOICE OF THERAPY	<a href="#"><u>4</u></a>
TYPE 2 DIABETES – MANAGEMENT ALGORITHM	<a href="#"><u>5</u></a>
TYPE 2 DIABETES – DOSE ADJUSTMENT IN RENAL /HEPATIC IMPAIRMENT	<a href="#"><u>6</u></a>
SGLT-2i FOR NON-DIABETIC INDICATIONS- HFrEF	<a href="#"><u>7</u></a>
CHECKLIST FOR INITIATING SGLT-2i	<a href="#"><u>8</u></a>
SGLT-2i PATIENT INFORMATION – TYPE DIABETES ONLY	<a href="#"><u>9</u></a>
CLASSIFICATION OF CKD IN ADULTS AND FREQUENCY OF MONITORING	<a href="#"><u>10</u></a>
ADDITIONAL GUIDANCE – GLP-1RA	<a href="#"><u>11</u></a>
TYPE 2 DIABETES – ADDITIONAL GUIDANCE	<a href="#"><u>12</u></a>
TYPE 2 DIABETES – RESEARCH EVIDENCE	<a href="#"><u>13</u></a>

These guidelines are dedicated to the memory of Dr Nick Lever of Barking Havering and Redbridge University Trust and Barts Health who sadly passed away unexpectedly in August 2022. We will always remember Dr Lever for his many contributions to these guidelines, and the field of nephrology across the East London.

# INDIVIDUALISATION OF PATIENT HbA1c TARGETS

Agree an individualised HbA1c target based on: the person's needs and circumstances including preferences, comorbidities, risks from polypharmacy and tight blood glucose control, and ability to achieve longer-term risk-reduction benefits. Support the person to aim for the agreed HbA1c target, measure HbA1c levels at:

- 3-6 monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy
- 6 monthly intervals once the HbA1c level and blood glucose lowering therapy are stable

Patients Group	Target HbA1c presumption (this must be individualised)
Patients managed by lifestyle and diet	<48% mmol/L (6.5%)
If <b>all</b> the following apply: <ul style="list-style-type: none"> <li>• Younger patients &lt;60years within 10 years of diagnosis</li> <li>• Without established macrovascular disease (IHD, CVA, PVD)</li> <li>• Taking a single oral agent not associated with the hypoglycaemia (metformin, DPP-4i, SGLT-2i, pioglitazone)</li> </ul>	48 mmol/L (6.5%)
If <b>all</b> the following apply: <ul style="list-style-type: none"> <li>• Younger patients &lt;60 years within 10 years of diagnosis</li> <li>• Without established macrovascular disease (IHD, CVA, PVD)</li> <li>• Without CKD</li> <li>• Low risk for serious consequence of hypoglycaemia</li> <li>• Taking SU/repaglinide/insulin/GLP-1 OR more than one oral agent</li> <li>• Without significant comorbidity</li> </ul>	53mmol/L (7.0%)
If life-expectancy > 10 years and <b>any</b> of the following apply: <ul style="list-style-type: none"> <li>• Age &gt;60 years or duration diabetes &gt;10 years</li> <li>• Established macrovascular disease (IHD, CVA, PVD)</li> <li>• CKD on dialysis</li> <li>• Tight control poses a high risk of the consequences of hypoglycaemia (e.g. risk of falling, impaired awareness of hypoglycaemia, people who drive or operate machinery as part of their job)</li> <li>• Experiences recurrent hypoglycaemia on SU/insulin</li> <li>• Significant comorbidities.</li> </ul>	58mmol/L (7.5%)
Patients who have moderate or severe frailty (the 'Rockwood Frailty Score' or the 'electronic Frailty Index' (eFI), which is integrated into EMIS, can be used to guide the clinicians judgement) and/or elderly (>80 years), and/or life-expectancy <10 years	<75mmol/L (<9%)

**Note:** Fructosamine may be more appropriate for monitoring diabetes if the following apply: sickle cell anaemia, other anaemia, homozygous haemoglobin variant disease or increased cell turnover. In these situations, fructosamine provides an alternate means of assessing glucose control. It gives an estimate of glucose control in the preceding 2 to 3 weeks. A level below of 340µmol/L indicates very good diabetes control and a level below 380µmol/L indicates good control. Seek advice from diabetes team.

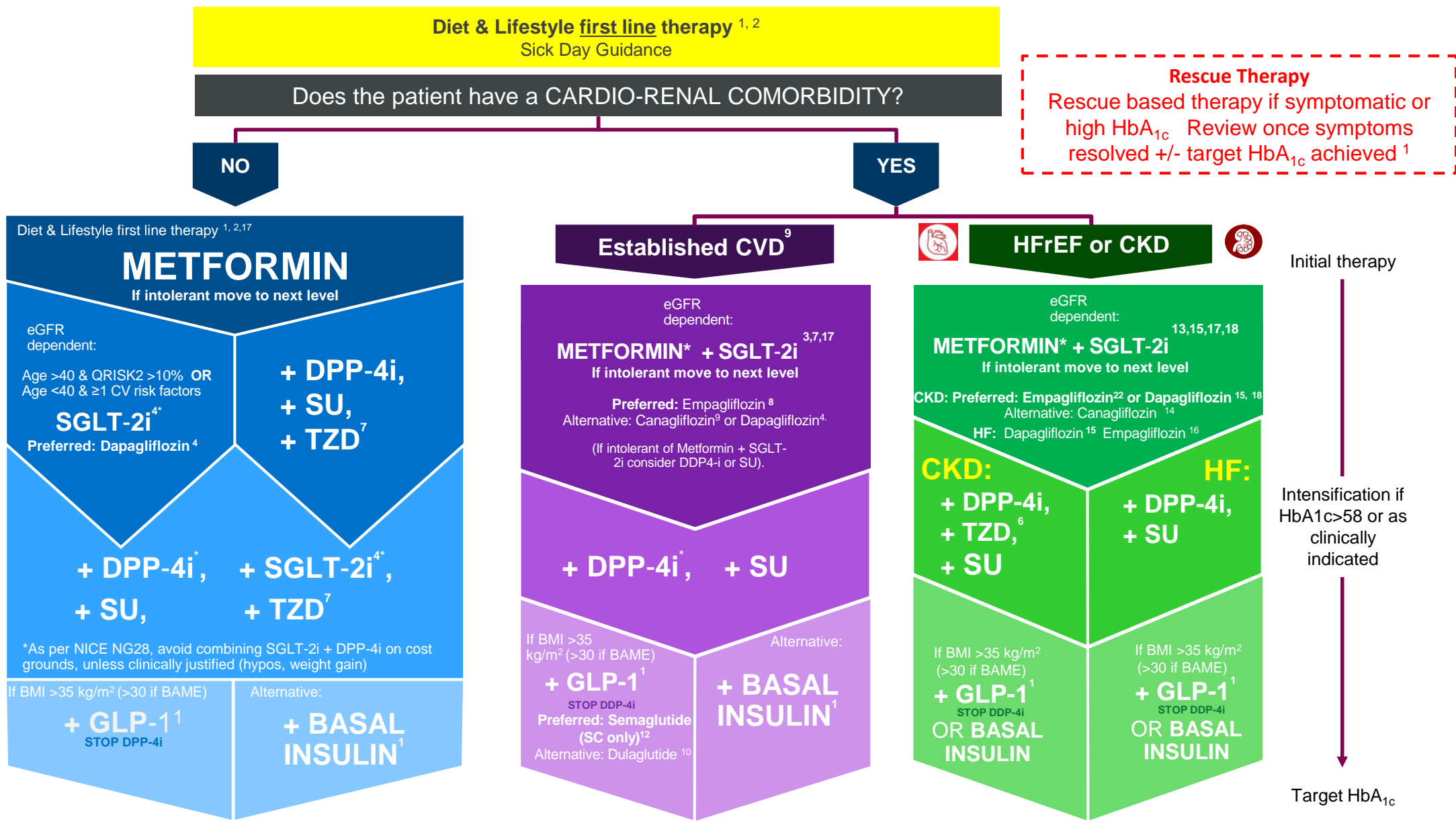


# PATIENT DECISION AID FOR CHOICE OF THERAPY

Issue	How important is this to me?			
	Very important	Important	Unimportant	Very unimportant
Getting to a lower target blood glucose (HbA1c) level				
How many tablets I would have to take and how often				
The possibility of getting hypos				
The possibility of gaining weight				
The possibility of other side effects				
Other concerns or questions I want to discuss with my healthcare professional				

*Adapted with permission from NHS City and Hackney*

# TYPE 2 DIABETES – MANAGEMENT ALGORITHM



<b>* When initiating metformin</b>	Consider 2 weeks of monotherapy before initiating another agent to assess for gastrointestinal side-effects
<b>When initiating a SGLT-2i</b>	Consider a 25% dose reduction in any concomitant SU or Basal insulin & monitor for evidence of hypoglycaemia
<b>GLP-1</b>	Consider discontinuing in those who do not achieve a beneficial metabolic response after 6 months (see additional guidance)
<b>Definitions</b>	DDP-4i (Dipeptidyl Peptidase-4 Inhibitor), SGLT-2i (Sodium Glucose Co-Transporter 2 Inhibitor), SU (Sulfonylurea), TZ (Thiazolidinedione) GLP-1 (Glucagon-like-peptide 1 analogues)

# TYPE 2 DIABETES – DOSE ADJUSTMENT IN RENAL /HEPATIC IMPAIRMENT

Drug	CKD stage 1 eGFR >90 mL/min	CKD stage 2 eGFR 60-90 mL/min	CKD stage 3a eGFR 45-59 mL/min	CKD stage 3b eGFR 30-44 mL/min	CKD stage 4 eGFR 15-29 mL/min	CKD stage 5 eGFR <15 mL/min	Mild to moderate hepatic impairment	Severe hepatic impairment
<b>Metformin</b>	✓	✓	✓	✓ Max 500mg BD	✗	✗	Specialist initiation only	✗
<b>Gliclazide</b>	✓	✓	✓	✓	Use lowest effective dose	✗	✓	✗
<b>Linagliptin</b>	✓	✓	✓	✓	✓	✓	✓	✓
<b>Sitagliptin</b>	100 mg	100 mg	100mg	50mg	25mg	25mg	✓	✗
<b>Alogliptin</b>	25mg	25mg	25mg	12.5mg	6.25mg	6.25mg	✓	✗
<b>Pioglitazone (TZD)</b>	✓	✓	✓	✓	✓	✓	✗	✗
<b>Dapagliflozin</b>	✓ Start 10mg	✓ Start 10mg	✓ Start 10mg	✓ Start 10mg (for T2D and CKD if eGFR 25 to 75mL/min)	✓ Start 10mg (for T2D and CKD if eGFR 25 to 75mL/min)	✓ Continue 10mg	✓	5mg
<b>Canagliflozin</b>	✓ Start 100- 300mg	✓ Start 100- 300mg	✓ Start 100mg	✓ Start 100mg, only	✓ Continue 100mg if UCAR>30mg/mm ol	✓ Continue 100mg if UCAR>30mg/m mol	✓	✗
<b>Empagliflozin</b>	✓ Start 10mg can be increased to 25mg	✓ Start 10mg can be increased to 25mg	✓ T2DM+CKD Start 10mg	✓ T2DM+CKD Start 10mg	✗ HF eGFR < 20: ✗ T2DM +CKD & eGFR ≥ 20: ✓ Start 10mg	✓ Continue 10mg for CKD	✓	✗
<b>Ertugliflozin</b>	✓ Start 5-15mg	✓ Start 5-15mg	✓ Start 5mg	✓ Continue 5mg	✗	✗	✓	✗
<b>Liraglutide</b>	✓	✓	✓	✓	✓	✗	✓	✗
<b>Semaglutide</b>	✓	✓	✓	✓	✓	✗	✓	Caution: limited information
<b>Dulaglutide</b>	✓	✓	✓	✓	✓	✗	✓	✓
<b>Tirzepatide</b>	✓	✓	✓	✓	✓	✓	✓	Caution: limited information
<b>Insulin</b>	✓	✓	✓	✓	✓	✓	✓	✓

**Be Aware:** Diminished glycaemic effect of SGLT-2i with eGFR < 45 mL/min, however sustained cardio-renal protection

**Key**

✓ Initiate    ✓ No new initiation unless for CKD or HF; continue at stated dose    ✗ Discontinue

**DPP4i**    **SGLT2i**    **GLP1 RA**

# SGLT-2i FOR NON-DIABETIC INDICATIONS- HFrEF

- Exclusion Criteria**  
A past medical history of:
- Type 1 diabetes
  - Systemic lupus erythematosus
  - Polycystic kidney disease

- Abbreviations**
- ACEi- angiotensin converting enzyme inhibitor
  - ARB- angiotensin receptor blocker
  - MRA- mineralocorticoid receptor blocker
  - LVEF- Left ventricular injection fraction
  - HR- Heart Rate
  - RAASi- Renin-angiotensin-aldosterone systems inhibitors (includes ACEi, ARB and MRAs)

Does the patient have Type 2 Diabetes?

YES

NO

**Refer to the Diabetes guidelines**

Does the patient have Heart Failure of Reduce Ejection Fraction (HFrEF) and/or Chronic Kidney Disease (CKD)?

**For CKD- refer to the CKD guidelines**

YES

Heart Failure diagnosed by specialist

Offer diuretics for the relief of congestive symptoms and fluid retention

Heart Failure with Reduced (HFrEF) or Preserved or mildly reduced (HFpEF) if symptoms persist after 1<sup>st</sup> line treatment

**First line:** Offer ACEi (consider ARB if intolerant) and Beta Blocker. Offer an MRA if symptoms continue

If symptoms persist despite optimal first line therapy, seek specialist advice

Specialist Review

**Add Licensed SGLT-2i** (if LVEF <40% or still symptomatic after 1<sup>st</sup> line treatment)  
If already established on an SGLT-2i switch to a licensed SGLT-2i

**Replace** ACEi (or ARB) with sacubitril valsartan (if LVEF<35%)

**Add ivabradine** If sinus rhythm, with a HR >75bpm and LVEF < 35%

**Add hydralazine & nitrate** (especially if of African/Caribbean descent)

**Add digoxin** for worsening heart failure

\*SGLT-2i

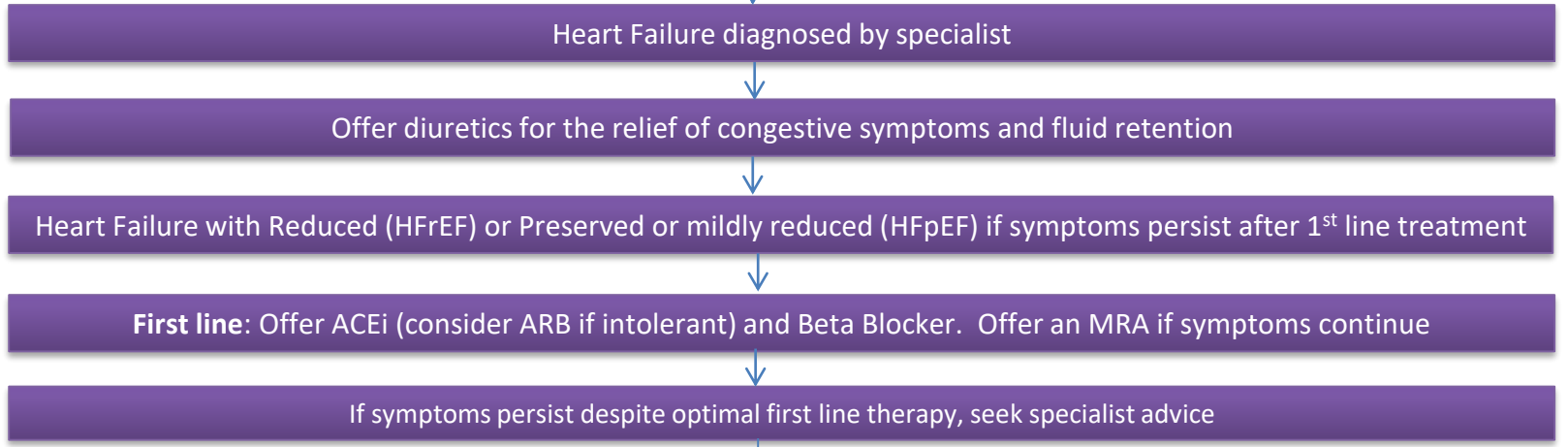
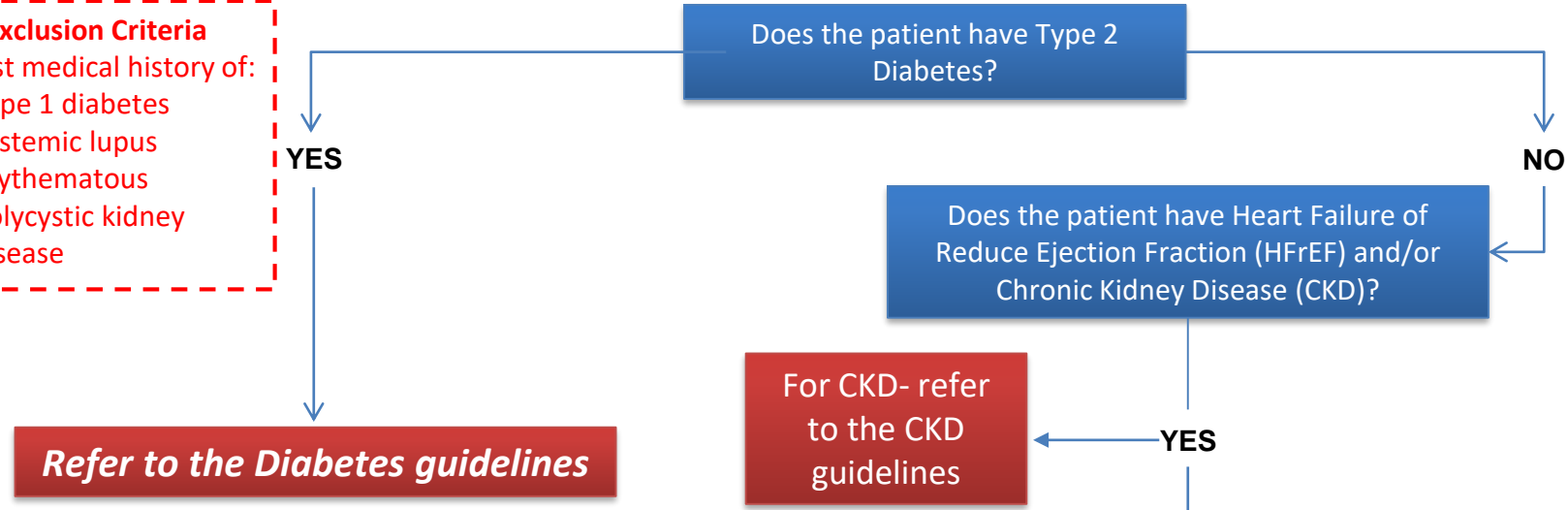
At the time of writing dapagliflozin and empagliflozin are the only SGLT-2i that have a UK license for the treatment of CKD or HFrEF without diabetes



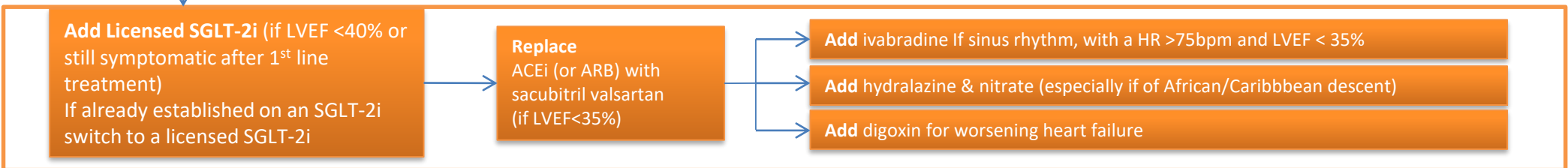
# SGLT-2i FOR NON-DIABETIC INDICATIONS- HFrEF

- Exclusion Criteria**  
A past medical history of:
- Type 1 diabetes
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- Abbreviations**
- ACEi- angiotensin converting enzyme inhibitor
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Specialist Review



\*SGLT-2i At the time of writing dapagliflozin and empagliflozin are the only SGLT-2i that have a UK license for the treatment of CKD or HFrEF without diabetes. Empagliflozin is also licensed for symptomatic chronic heart failure with preserved (HFpEF) or mildly reduced ejection fraction in adults without diabetes.

# CHECKLIST FOR INITIATING SGLT-2i (canagliflozin, empagliflozin, dapagliflozin & ertugliflozin)

## Contraindications

- Type 1 diabetes
- Patients <18 years ≥85years
- Pregnancy and breastfeeding (counsel patients of childbearing potential on the risks of taking a SGLT-2i during pregnancy)
- Previous DKA whilst taking a SGLT-2i

## Cautions

- Risk of volume depletion, especially in elderly or frail patients- review diuretics
- Consider reduction of dose of sulfonylurea/repaglinide/insulin or speak to specialist for advice
- Tablets contain lactose, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## DKA risk factors

- Low beta cell function (e.g. low C-peptide levels, latent autoimmune diabetes in adults [LADA], a history of pancreatitis)
- Restricted food intake or severe dehydration.
- Sudden reduction in insulin
- Surgery
- Alcohol dependence

**Seek specialist advice or consider alternative options if patient is at risk of DKA**

## Monitoring Requirements

- Check HbA1c, weight and BP before initiating
- Assess liver function
- Assess renal function before treatment , unlike ACEi/ARB there is no need to check renal function after initiation.
- In the elderly there is a risk of hypotension, assess frailty with an approved frailty score and review antihypertensive if necessary.

*Initial increases in creatinine and initial decrease in eGFR are generally transient during initiation or reversible after discontinuation.*

## Patient Advice

- SGLT-2i reduce blood glucose by preventing the kidneys from reabsorbing glucose back into the blood so excess glucose is passed out in the urine.
- Risk of DKA and symptoms (vomiting, nausea, abdominal pain, a sweet smell to the breath, confusion etc) and seek urgent medical help.
- Sick day rules- stop temporarily during acute illness, vomiting or diarrhoea.
- Common adverse reactions such as polyuria, genital infection and UTI; advise to use clotrimazole 1% cream (can be bought OTC) if symptoms of genital candida develop. Advise on good genital hygiene.
- Individuals taking diuretics should be counselled on the symptoms of hypovolaemia and when to seek medical advice.
- Importance of foot care.
- If Fournier's gangrene is suspected, stop the SGLT-2i and seek urgent medical advice. (NOTE this is extremely unlikely i.e. less than 1 in 10,000 chance and only applies to patients with T2DM)

## What are SGLT-2i's?

- SGLT2 inhibitors are a class of drugs used in the treatment of diabetes but also are used to keep the kidneys and heart healthy.
- They are available in tablet form and usually taken once daily.
- They may be prescribed on their own or in combination with other diabetes medications including insulin.
- They help lower blood glucose level by reducing the reabsorption of glucose in the kidneys and allowing glucose to be passed out in the urine

## Who are SGLT-2i's suitable for?

This medication is used for the treatment of type 2 diabetes. To prevent kidney and heart complications. Before starting this medication tell your doctor/diabetes specialist nurse if you have the following conditions:

- Previous history of diabetic ketoacidosis (DKA).
- Problems with recurrent urinary tract infections.
- Problems with recurrent genital infections. ('thrush').
- History of peripheral vascular disease.
- Alcohol dependency.
- Planning or are pregnant or breastfeeding.

If you have any of the above conditions, SGLT2 inhibitor may not necessarily be suitable for you.

## What are the benefits of SGLT-2i's?

- Improvement in blood glucose.
- Weight loss.
- Lowering of blood pressure.
- Lowering risks of death in people with heart disease
- Keeping the kidneys and heart healthy over time

## What are the possible side effects of SGLT2 inhibitors?

### Very common ( $\geq 1/10$ )

An increase in the risk of hypoglycaemia when used in combination with other diabetes medication (insulin/sulfonylurea).

### Common ( $\geq 1/100$ to $< 1/10$ )

- Developing genital or urinary tract infections.
- Passing more urine more often.
- Increased thirst.
- Itching/rash.

### Uncommon ( $\geq 1/1,000$ to $< 1/100$ )

- Getting low blood pressure and dehydration.
- Difficulty passing urine (dysuria).

### Rare ( $\geq 1/10,000$ to $< 1/1,000$ )

- Diabetic ketoacidosis (rare but serious side effect).
- Necrotising fasciitis of the perineum (Fournier's gangrene) [pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise].

## What is diabetic ketoacidosis (DKA)?

- DKA is rare but serious condition that can develop in people who have diabetes. It is a serious condition which requires urgent medical treatment. Less than 1 in 1000 people on an SGLT-2i experience DKA.
- DKA usually occurs when the body does not have enough insulin, this results in the formation of ketone bodies leading to increasing levels of acid in the blood.
- Symptoms can include nausea and vomiting, abdominal/stomach pain, rapid breathing, dehydration e.g. dizziness and excessive thirst, a sweet metallic taste in the mouth or a different odour the urine or sweat, drowsiness or tiredness and/or confusion.

# CLASSIFICATION OF CKD IN ADULTS AND FREQUENCY OF MONITORING

Use the table below to guide the minimum frequency of eGFR creatinine but tailor to the individual patient according to the underlying cause of CKD, the rate of decline in eGFR or increase in ACR (note progression may not be linear), other risk factors (heart failure, diabetes and hypertension), changes to treatment (such as ACEi/ARBs, diuretics & NSAIDs), intercurrent illness and if a patient has chosen conservative management for their CKD.

<b>Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012</b>				<b>Persistent albuminuria categories</b>		
				Description and range		
				<b>A1</b>	<b>A2</b>	<b>A3</b>
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
<b>GFR categories (ml/min/1.73 m<sup>2</sup>)</b> Description and range	<b>G1</b>	Normal or high	≥ 90	Monitor 0 to 1 times a year	Monitor once a year	Monitor 1 or more times a year
	<b>G2</b>	Mildly decreased	60–89	Monitor 0 to 1 times a year	Monitor once a year	Monitor 1 or more times a year
	<b>G3a</b>	Mildly to moderately decreased	45–59	Monitor once a year	Monitor once a year	Monitor 2 times a year
	<b>G3b</b>	Moderately to severely decreased	30–44	Monitor 1 to 2 times a year	Monitor 2 times a year	Monitor 2 or more times a year
	<b>G4</b>	Severely decreased	15–29	Monitor 2 times a year	Monitor 2 times a year	Monitor 3 times a year
	<b>G5</b>	Kidney failure	< 15	Monitor 4 times a year	Monitor 4 or more times a year	Monitor 4 or more times a year

# ADDITIONAL GUIDANCE – GLP-1RA

## Treatment priority

Weight loss as a secondary benefit of glucose lowering therapy

Primary CV risk reduction (if high risk of CVD)

Secondary CV risk reduction (if established CVD)

### Semaglutide subcutaneous (once weekly)

28 days supply = 1 box of 1 pen, each pen contains four doses.

### Tirzepatide subcutaneous (once weekly)

28 days supply = either single use vials (each vial = one dose) or KwikPen = each pen contains four doses.

### Semaglutide oral (once daily)

- Use S/C Semaglutide wherever possible as greater efficacy and proven CV benefit. Oral Semaglutide should only be considered for patients who are unable to receive GLP-1 in an injectable form.
- Confirm person can adhere to the fasting administration requirement (no tea, coffee, milk, food, other medicines for 30 minutes after dosing) and an increase in total daily dosing frequency

### Dulaglutide (once weekly)

28 days supply = 1 box of 4 pens, each pen contains one dose.

### Liraglutide (once a day)

28 days supply = 1 box of 2 pens, each pen 18mg in 3ml

### Semaglutide subcutaneous (once weekly)

28 days supply = 1 box of 1 pen, each pen contains four doses.

### Dulaglutide (once weekly)

28 days supply = 1 box of 4 pens, each pen contains one dose.

### Liraglutide (once a day)

28 days supply = 1 box of 2 pens, each pen 18mg in 3ml

#### Definitions

Established CVD:

- Evidence of prior cardiovascular event (e.g. MI/stroke/UA),
- Prior coronary, carotid or peripheral arterial revascularisation or peripheral vascular disease
- Proven myocardial ischaemia

High risk of CVD:

- Absence of established CVD, **and**
- CVD risk factors including but not limited to:
  - coronary, carotid or lower extremity artery stenosis
  - eGFR persistently <60 mL/min/1.73 m<sup>2</sup>
  - hypertension with left ventricular hypertrophy; or persistent albuminuria

#### Starting Dose & Titration

- S/C Dulaglutide 1.5 mg OW; if required maybe titrated by 1.5 mg every 4 weeks as tolerated to a maximum dose 4.5 mg OW
- S/C Liraglutide 0.6mg OD for at least 1 week, then increased to 1.2mg SC once a day for at least 1 week, then increased if necessary to 1.8mg SC once a day.
- S/C Semaglutide 0.25mg OW, up titrate every 4 weeks to maximum dose 1 mg OW
- PO Semaglutide 3mg OD, up titrate to 7mg after 1-month, maximum dose 14 mg OD if required
- S/C Tirzepatide 2.5mg OW, up titrate by 2.5mg every 4 weeks. The maximum dose is 15 mg once weekly.

#### NICE Recommendations for GLP-1 agonist therapy

- BMI  $\geq 35$  (adjust according to ethnicity) & specific psychological or other medical problems
- Have a BMI <35 and for whom insulin would have a significant occupational hazards.
- Have a BMI <35 for who weight loss would benefit other significant obesity-related comorbidities.

# TYPE 2 DIABETES – ADDITIONAL GUIDANCE

## Sick Day Guidance – to be reiterated to patients at every opportunity

### When unwell (acute illness):

Fever, sweats, shaking  
Vomiting / diarrhoea  
Unable to eat or drink

### Miss out / Omit / Pause:

**S** – SGLT-2i  
**A** – ACEi  
**D** – Diuretics  
**M** – Metformin  
**A** – ARBs  
**N** - NSAIDs

### After 2-3 days:

Feeling better = Restart paused medicines

Not better = seek medical attention

Increase blood glucose monitoring during acute illness and check for ketones. If you are using daily insulin or a SUs, you may need to increase (or decrease) the amount taken to maintain appropriate glucose control. Ensure fluid intake to minimise dehydration.

Adapted from Imperial College Healthcare NHS Trust Renal Sick Day Rules

## Lifestyle Counselling – to be reiterated to patients at every opportunity

### Dietary Guidance

Seek dietitian input. Individualised approach: low fat diet, low Glycaemic Index diet or Mediterranean diet etc. Alternatives include low calorie total diet replacement programmes (NWL REWIND).

### Physical Activity

Realistic targets should be set. The benefits of regular exercise should be explained and people should be advised to perform regular aerobic activity. Clinical studies show that walking for 30 minutes every day has cardiovascular benefits.

### Weight Management

Weight loss can help the patient achieve Type 2 diabetes remission. Realistic initial weight loss target of 5% to 10% of starting weight. Consider drug therapy, e.g SGLT-2i or GLP-1. Consider surgical intervention.

### Smoking Cessation & Alcohol consumption

Assess patients for smoking status and refer to Smoking Cessation Teams for support. Alcohol may influence blood glucose control (Hyper/Hypo glycaemia respectively).

## Medication review

Reassess the person's needs and circumstances at each review (3-6 months) and think about whether to stop any medicines that are not effective.

[Adjustments for Renal & Hepatic Impairment](#)

### GLP-1

Only continue in those with a beneficial metabolic response after **6 months** (reduction of  $\geq 11$  mmol/mol [1.0%] in HbA1c and weight loss of  $\geq 3\%$  of initial body weight).

### SGLT-2i

Stop & reassess if complicated by active foot ulcer or DKA (could be euglycemic).

### DPP-4i

Not to be used in conjunction with GLP-1.

### TZD

Stop in the event of HF, DKA or bladder cancer.

### SU

In the event of significant hypos, stop & reassess.

# TYPE 2 DIABETES – RESEARCH EVIDENCE

Given the recent wealth of publications regarding cardiovascular & renal outcome trials in type 2 diabetes, this Type 2 Diabetes Management Algorithm is meant as a quick reference guide as we move away from glucose-centric prescribing, based on current evidence as of August 2022. For more in-depth guidance please refer to the [EASD-ADA Consensus Document](#), or other [inter]national guidelines. [Also see CaReMe multi-association position statement](#).

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Lifestyle management should be part of the on-going discussion with individuals with T2DM at each visit. Increasing physical activity and reducing body weight improves glycaemic control and should be encouraged in all people with T2DM<sup>1</sup>. Glycaemic treatment targets should be individualised based on patient preferences and patient characteristics, including frailty and comorbid conditions<sup>1</sup>. All drugs can cause side effects, consult BNF or summary of product characteristics for full side effect profile of individual drugs. Always offer advice on sick day guidance for patients on Metformin and/or SGLT-2i<sup>1</sup>. Stop SGLT-2is peri-operatively or if restricted food intake or dehydration<sup>1</sup>. Patients on insulin treatment should always be advised never to stop or significantly reduce their insulin as part of the sick day response<sup>1</sup>. SU & TZD both have low acquisition cost, this should be taken into consideration alongside increased risk of weight gain and hypoglycaemia risk (SU).

## Abbreviations:

T2DM; type 2 diabetes mellitus, eGFR, estimated glomerular filtration rate; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; DPP-4i, dipeptidyl peptidase 4 inhibitor (gliptin); SU, sulfonylurea; TZD, thiazolidinedione; BMI, body mass index; GLP-1, glucagon-like peptide-1 receptor agonist; +ive, positive; CVD, cardiovascular disease; eCVD, established cardiovascular disease; MI, myocardial infarction; HF, heart failure; CKD, chronic kidney disease with eGFR < 60; HbA<sub>1c</sub>, haemoglobin A1C; BD, twice daily; ACEi, Angiotensin-converting enzyme inhibitors; ARB, Angiotensin II receptor blocker; NSAID, Non-steroidal anti-inflammatory drug; DKA, diabetic ketoacidosis; uACR, urine albumin creatinine ratio; HFrEF, Heart Failure with reduced Ejection Fraction, MRA, mineral receptor antagonist.

## References:

1. [North West London Diabetes Guidelines](#) (Adapted with permission)
2. DiRECT; Lancet 2018; 391: 541–51 [https://doi.org/10.1016/S0140-6736\(17\)33102-1](https://doi.org/10.1016/S0140-6736(17)33102-1)
3. When prescribing an SGLT-2i, consider risk of volume depletion, euglycemia DKA in insulin deficient cohorts and lower limb amputation (class warning, but only observed in Cana and Eurtu). Caution in frail patients and always follow sick day rules. For more information, refer to full [North West London Diabetes Guidelines](#)
4. DECLARE TIMI 58; N Engl J Med 2019; 380:347-357; DOI: <https://doi.org/10.1056/NEJMoa1812389>
5. FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin <https://bit.ly/2ZZCNni>
6. TZD (Pioglitazone) to be avoided in patients with heart failure. PROactive; Lancet. 2005 Oct 8;366(9493):1279-89 [https://doi.org/10.1016/S0140-6736\(05\)67528-9](https://doi.org/10.1016/S0140-6736(05)67528-9)
7. Consider initiating Met + SGLT-2i rather than stepwise. This is in line with Position Statement by Primary Care Diabetes Europe; S. Seidu, et al., A disease state approach to the pharmacological management of Type 2 diabetes in primary care: A position statement by Primary Care Diabetes Europe, Prim. Care Diab. (2020), <https://doi.org/10.1016/j.pcd.2020.05.004>. Alternatively, the European Society of Cardiology (ESC) diabetes guideline states that SGLT-2i could be considered as first line ahead of metformin in patients with eCVD, HF or CKD - European Heart Journal (2019) 00, 169; doi: <https://doi.org/10.1093/eurheartj/ehz486>
8. EMPA-REG; N Engl J Med 2015; 373:2117-2128; DOI: <https://doi.org/10.1056/NEJMoa1504720>
9. CANVAS; N Engl J Med 2017; 377:644-657; DOI: <https://doi.org/10.1056/NEJMoa1611925>
10. PIONEER 6; N Engl J Med 2019; 381:841-851; DOI: <https://doi.org/10.1056/NEJMoa19011186>
11. SUSTAIN 6; N Engl J Med. 2016 Nov 10;375(19):1834-1844 DOI: <https://doi.org/10.1056/NEJMoa1607141>
12. ABCD SGLT-2i & GLP-1 Position Statement (2021) Basu, et al. *BJD*. 2021; 21(1): 132-148 <https://bit.ly/3zXBWmf>
13. DAPA HF; September 19, 2019; DOI: <https://doi.org/10.1056/NEJMoa1911303>
14. CREDENCE; N Engl J Med 2019; 380:2295-2306; DOI: <https://doi.org/10.1056/NEJMoa1811744>
15. DAPA CKD; N Engl J Med 2020; 383:1436-1446; DOI: <https://doi.org/10.1056/NEJMoa2024816>
16. EMPOROR REDUCED; N Engl J Med 2020; 383:1413-1424 DOI: <https://doi.org/10.1056/NEJMoa2022190>
17. National Institute for Health and Care Excellence (2022). Type 2 diabetes in adults: management [NICE guideline NG28] <https://www.nice.org.uk/guidance/ng28>
18. UK Kidney Association Clinical National Institute for Health and Care Excellence (2021). Chronic kidney disease assessment and management [NICE guidelines NG203] <https://www.nice.org.uk/guidance/ng203>
19. Practice Guideline: Sodium-Glucose Co-Transporter-2 (SGLT-2) inhibition in Adults with Kidney Disease (2021) [https://ukkidney.org/sites/renal.org/files/UKKA%20guideline\\_SGLT2i%20in%20adults%20with%20kidney%20disease%20v1%2020.10.21.pdf](https://ukkidney.org/sites/renal.org/files/UKKA%20guideline_SGLT2i%20in%20adults%20with%20kidney%20disease%20v1%2020.10.21.pdf)
20. Tirzepatide for treating type 2 diabetes- Technology appraisal guidance [TA924]Published: 25 October 2023: <https://www.nice.org.uk/guidance/ta924>
21. Tirzepatide Once Weekly for the Treatment of Obesity: N Engl J Med 2022; 387:205-216 DOI: 10.1056/NEJMoa2206038
22. Empagliflozin in Patients with Chronic Kidney Disease The EMPA-KIDNEY Collaborative Group\* <https://www.nejm.org/doi/full/10.1056/NEJMoa2204233>