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Diabetes Update

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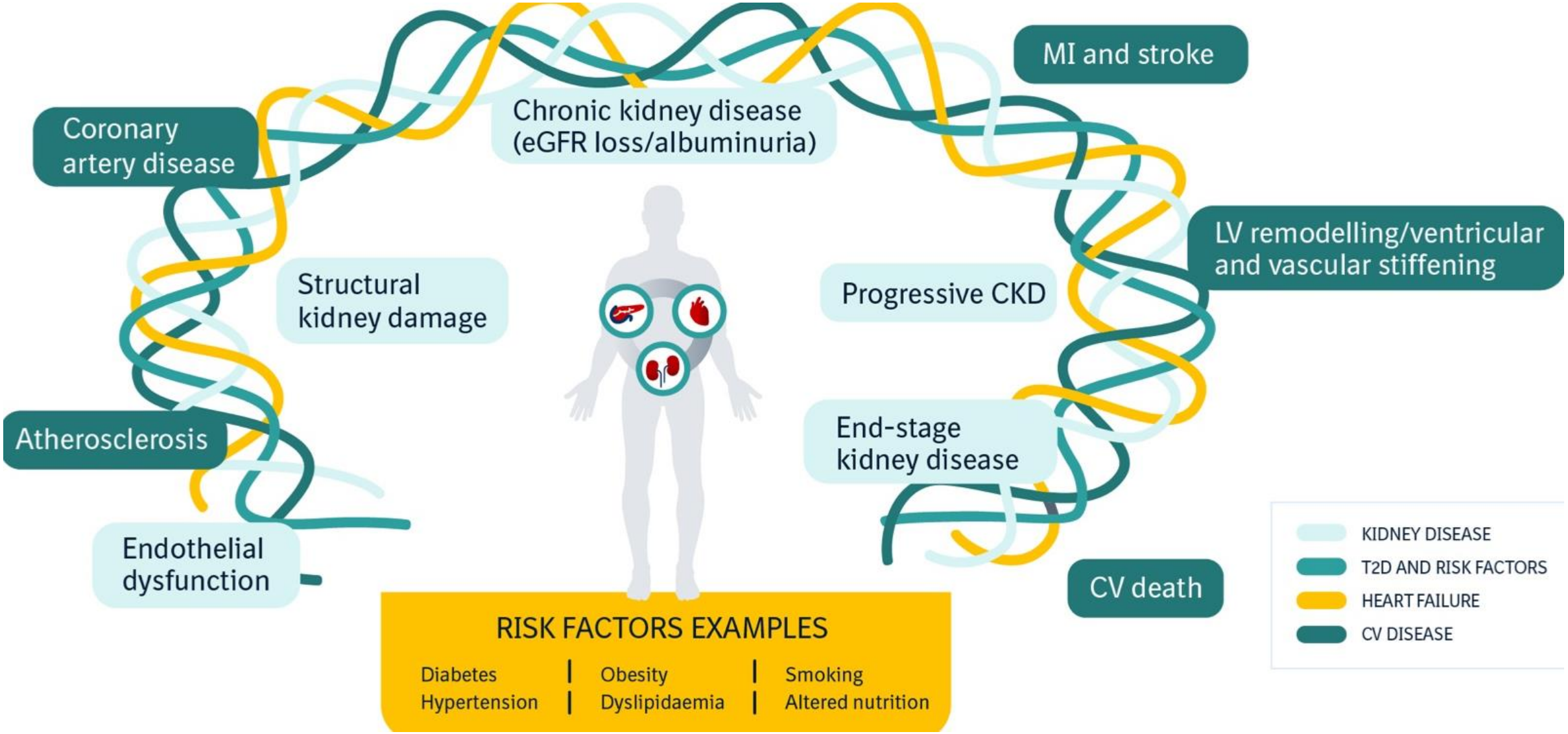
Medicines Optimisation Webinar

Wednesday 15th June 2022

Content

1. NICE update to Type 2 Diabetes in Adults [NG 28]
2. Prescribing SGLT2s safely
3. Diabetes and Frailty
4. Recognising hypoglycaemia
5. Insulin formulary
6. Prescribing Information and where to get advice
7. NICE update to monitoring of glucose levels
8. Educational opportunities

Aims of Treatment



Complications of Diabetes

Microvascular (small blood vessels)

Retinopathy

Neuropathy

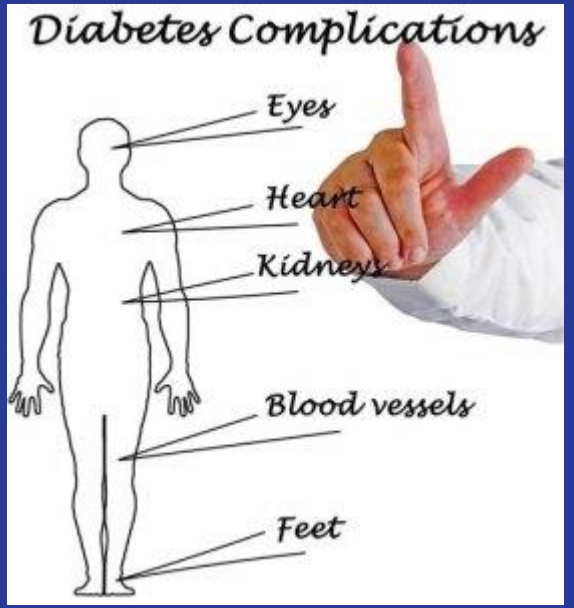
Nephropathy

Macrovascular (large blood vessels)

Stroke

Myocardial Infarction

Peripheral arterial disease



Diabetes

Three Treatment Targets

	QoF target
Blood Pressure	<140/80 mmHg
HbA1c	<58 mmol/mol (without frailty) <75 mmol/mol (with frailty)
Cholesterol	Total cholesterol <5 mmol/L

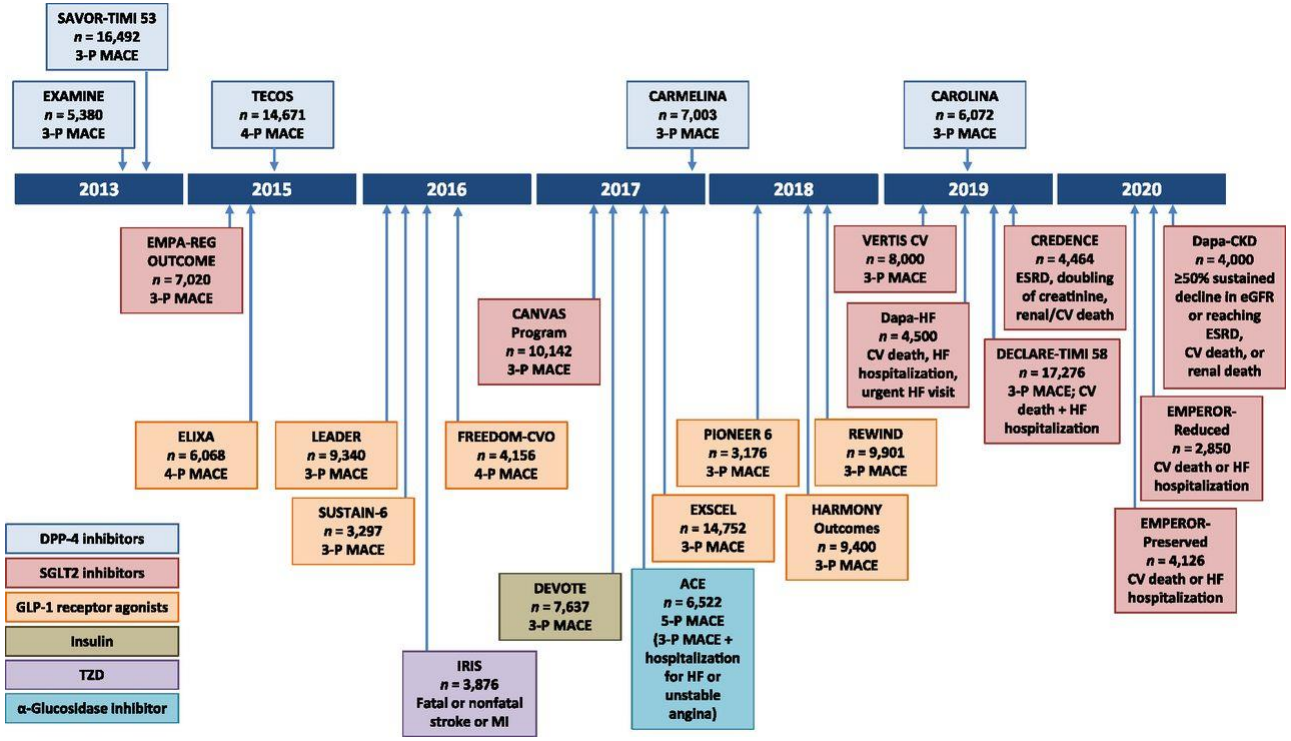
Information taken from the NDA shows that attainment of all 3 treatment targets in T2 diabetes was around a third for 2021.

NICE Guidance Type 2 Diabetes

Feb 22

Cardiovascular Outcome Trials (CVOTs)

Following concerns about the cardiovascular safety of Rosiglitazone, now mandated that glycaemic agents have acceptable CV risk profiles.

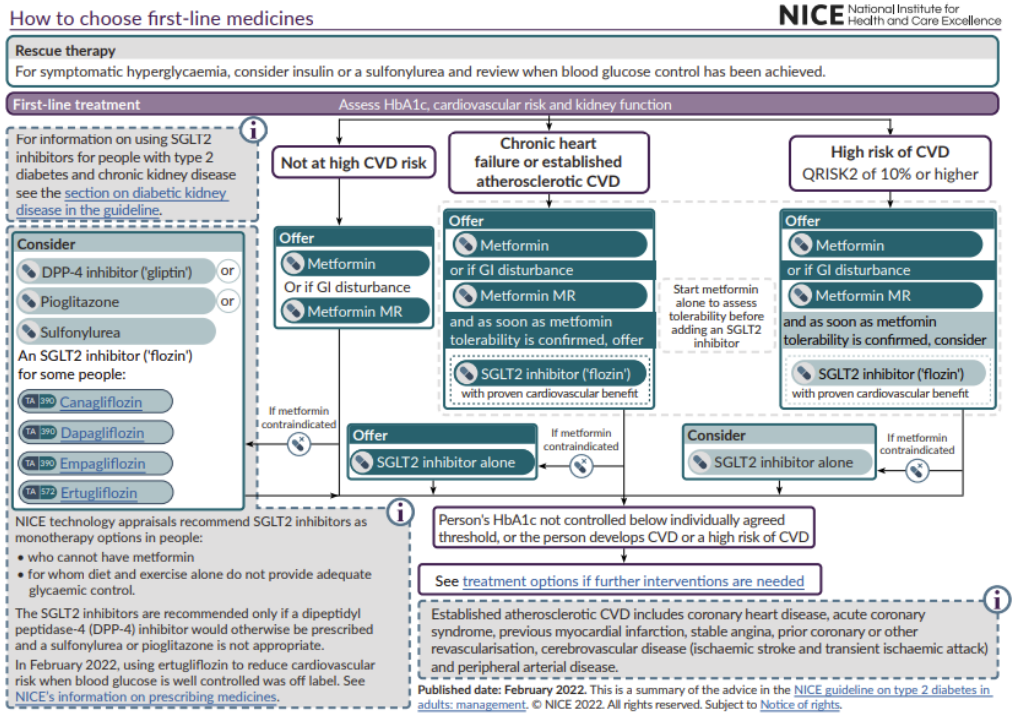


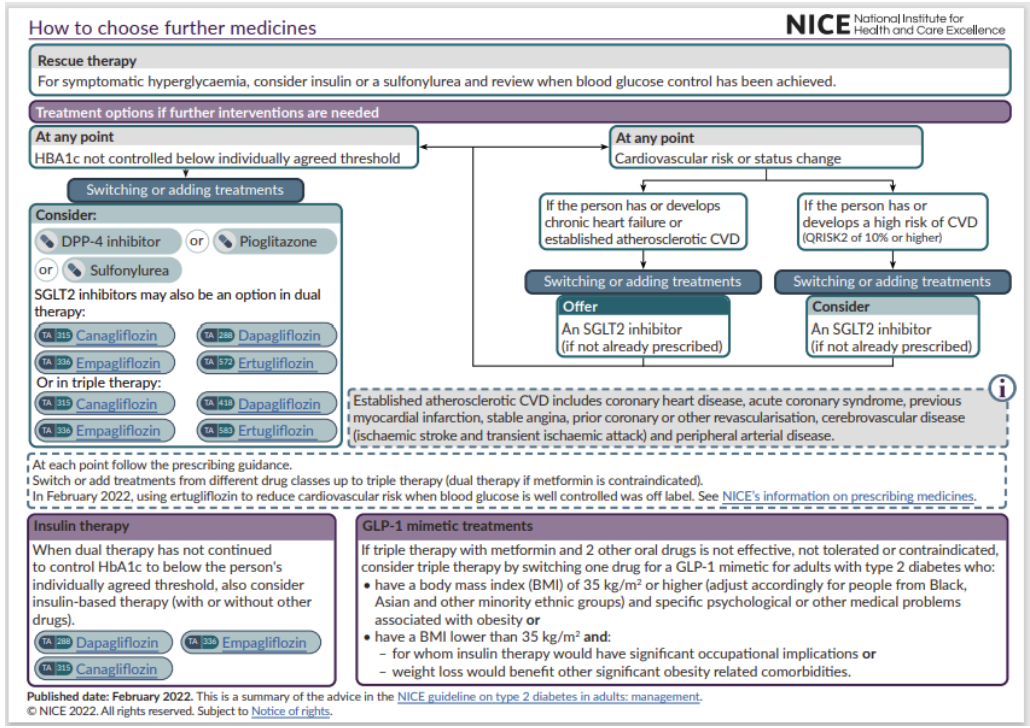
What have we learned?

Evidence from the CVOTs showed that SGLT2 inhibitors demonstrated favourable outcomes in relation to cardiovascular events.

Other agents, such as DPP-4 inhibitors (“gliptins”), sulfonylureas and insulin did not show this benefit.

Type 2 Diabetes in Adults: Management [NG28]





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SGLT2 Inhibitors

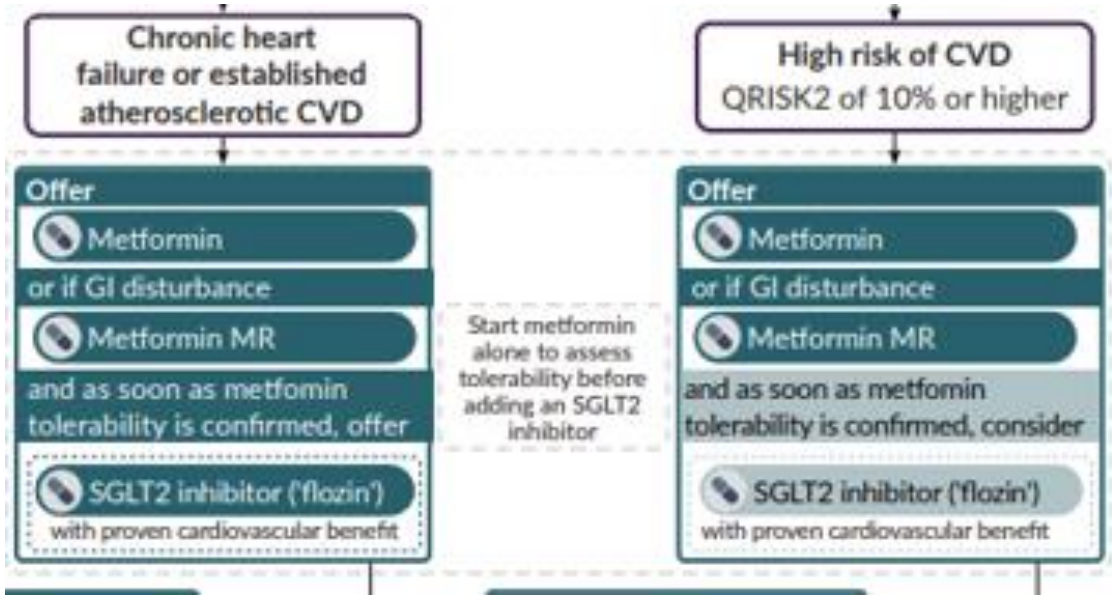
First line alongside Metformin for vast majority of people.

Independent of HbA1c.

Proven cardiovascular benefit (not Ertugliflozin).

Consider Dapagliflozin.

“Offer” or “Consider”



SGLT2 Inhibitors for High Risk of CVD with Type 2 Diabetes

Calculating Cardiovascular Risk

If they are at high risk of developing cardiovascular disease, consider an SGLT2 inhibitor with proven cardiovascular benefit in addition to metformin. [NG28]

QRisk2

A tool to provide an estimate of a person's cardiovascular risk over the next 10 years.

QRisk2 within current clinical systems and suggested by current NICE guidance.

Not to be used in secondary prevention, type 1 diabetes or with eGFR<60 +/ albuminuria

QRisk® 2 will underestimate risk in some cases, so clinical judgement required (HIV treatment, serious mental health problems, antipsychotics, corticosteroids or immunosuppressants, autoimmune disorders e.g. systemic lupus erythematosus).

SGLT2 Inhibitors for Atherosclerotic Cardiovascular Disease for Type 2 Diabetes

Coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, prior coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack) and peripheral arterial disease.

If they have chronic heart failure or established atherosclerotic cardiovascular disease, offer an SGLT2 inhibitor with proven cardiovascular benefit in addition to metformin. [NG 28]

SGLT2 Inhibitors for CKD with or without Type 2 Diabetes

NICE TA 775 Dapagliflozin for treating CKD

Standard Care: Diet and Lifestyle and ACE/ARB (where uACR>3mg/mmol) to maximum tolerated dose

Strong evidence from RCTs showed that SGLT2 inhibitors reduced the risk of CKD progression, mortality and cardiovascular events in adults with type 2 diabetes and CKD.

> ***it is an add-on to optimised standard care ….and people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m2 to 75 ml/min/1.73 m2 at the start of treatment and have type 2 diabetes or have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more. [TA 775]***

SGLT2 Inhibitor Comparison

Indications, doses and starting/stopping recommendations of SGLT2 inhibitors, by drug name.

Drug	Indication	Drug and dose	Initiate	Stop/reduce	Notes
Canagliflozin	Insufficiently controlled type 2 diabetes	Canagliflozin 100 mg Increase to **300 mg** if required	eGFR ≥45* eGFR ≥60	eGFR persistently <45* Reduce to 100 mg if eGFR <60	*Licensed for initiation to eGFR ≥30 but reduced glucose lowering below eGFR 45; add another glucose-lowering drug if needed
	Diabetic kidney disease (DKD)	Canagliflozin 100 mg	eGFR ≥30	eGFR persistently <30 and ACR <30 mg/mmol Can continue to dialysis/transplant if ACR ≥30 mg/mmol	Add on to standard of care (e.g. ACEi or ARB) for DKD
Dapagliflozin	Insufficiently controlled type 2 diabetes	Dapagliflozin 10 mg	eGFR ≥45†	eGFR persistently <45†	†Licensed for initiation to eGFR ≥15 but reduced glucose lowering below eGFR 45; add another glucose-lowering drug if needed
	Diabetic/chronic kidney disease (DKD/CKD)	Dapagliflozin 10 mg	eGFR ≥15	No lower eGFR limit. Specialist discussion as dialysis/transplant approaches	Use with other DKD/CKD therapies. With or without type 2 diabetes
	Symptomatic chronic HFrEF	Dapagliflozin 10 mg	eGFR ≥15	No lower eGFR limit. Specialist discussion as dialysis/transplant approaches	With or without type 2 diabetes
Empagliflozin	Insufficiently controlled type 2 diabetes	Empagliflozin 10 mg Increase to **25 mg** if required	eGFR ≥60‡ eGFR ≥60	eGFR persistently <45‡ Reduce to 10 mg if eGFR <60	‡Licensed for initiation to eGFR ≥30 in those with established CVD but reduced glucose lowering below eGFR 45; add another glucose-lowering drug if needed
	Symptomatic chronic HFrEF	Empagliflozin 10 mg	eGFR ≥20	eGFR <20; should not be used in those with end-stage renal disease or on dialysis	With or without type 2 diabetes
Ertugliflozin	Glycaemic control	Ertugliflozin 5 mg Increase to **15 mg** if required	eGFR ≥60 eGFR ≥60	eGFR persistently <45 eGFR persistently <45	eGFR <45, reduced glucose-lowering; add another glucose-lowering drug if needed

eGFR presented in mL/min/1.73 m².
ACEi=angiotensin-converting enzyme inhibitor; ACR=albumin:creatinine ratio; ARB=angiotensin receptor blocker; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; HFrEF=heart failure with reduced ejection fraction.

Note: Licences for some drugs in this list may differ in Northern Ireland. **This advice is for HCPs in Great Britain only.**
Information correct on 18th February 2022. **Licence amendments pending – view most recent version.**
Always consult the electronic BNF or the Summaries of Product Characteristics (SPCs) prior to prescribing any drug.
SPCs: Canagliflozin | Dapagliflozin | Empagliflozin | Ertugliflozin

Prescribing SGLT2 Inhibitors Safely

Cautions and Contraindications

DKA

Ketogenic or very low carbohydrate diet

Currently unwell

Pregnancy/breastfeeding

Type 1 Diabetes

Persistent/complicated UTI

Frail and elderly

Guidance awaiting approval at APC (June 22)

Side Effects of SGLT2s

SGLT2 inhibitors cause glucose to be removed from the body through urine – UTI/fungal infections.

Fournier's Gangrene (necrotising fasciitis of the perineum) a very rare side effect but ensure counselled on need for immediate review.

Diabetic ketoacidosis (risk of euglycaemic DKA increased)

Dehydration (thirst, hypotension)

Weight loss

BP reduction

The risk of DKA must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level.

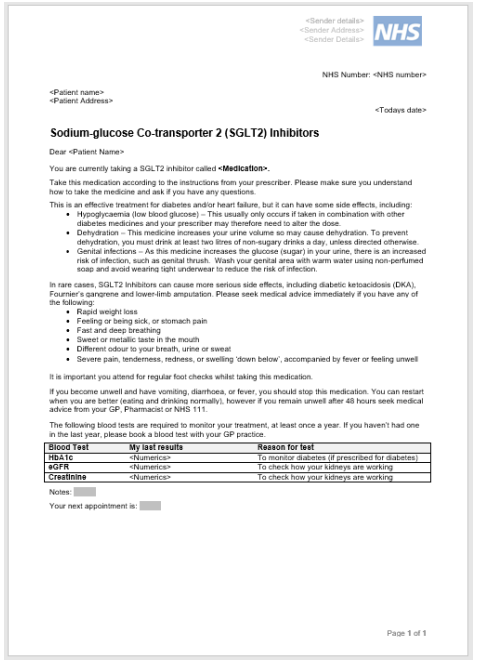
SGLT2 Inhibitor Counselling

Written Information

Sick day rules – stop SGLT2 inhibitor if diarrhoea or vomiting or symptoms suggestive of DKA. SGLT2 inhibitors:updated advice on the risk of DKA

Staying hydrated

Potential side effects including Fournier's Gangrene and risk of euglycaemic DKA. MHRA alert



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NHS

NHS Number: <NHS number>

<Patient name>
<Patient Address>

<Todays date>

Sodium-glucose Co-transporter 2 (SGLT2) Inhibitors

Dear <Patient Name>

You are currently taking a SGLT2 inhibitor called **<Medication>.**

Take this medication according to the instructions from your prescriber. Please make sure you understand how to take the medicine and ask if you have any questions.

This is an effective treatment for diabetes and/or heart failure, but it can have some side effects, including:

- Hypoglycaemia (low blood glucose) – This usually only occurs if taken in combination with other diabetes medicines and your prescriber may therefore need to alter the dose.
- Dehydration – This medicine increases your urine volume so may cause dehydration. To prevent dehydration, you must drink at least two litres of non-sugary drinks a day, unless directed otherwise.
- Genital infections – As this medicine increases the glucose (sugar) in your urine, there is an increased risk of infection, such as genital thrush. Wash your genital area with warm water using non-perfumed soap and avoid wearing tight underwear to reduce the risk of infection.

In rare cases, SGLT2 Inhibitors can cause more serious side effects, including diabetic ketoacidosis (DKA), Fournier's gangrene and lower-limb amputation. Please seek medical advice immediately if you have any of the following:

- Rapid weight loss
- Feeling or being sick, or stomach pain
- Fast and deep breathing
- Sweet or metallic taste in the mouth
- Different odour to your breath, urine or sweat
- Severe pain, tenderness, redness, or swelling 'down below', accompanied by fever or feeling unwell

It is important you attend for regular foot checks whilst taking this medication.

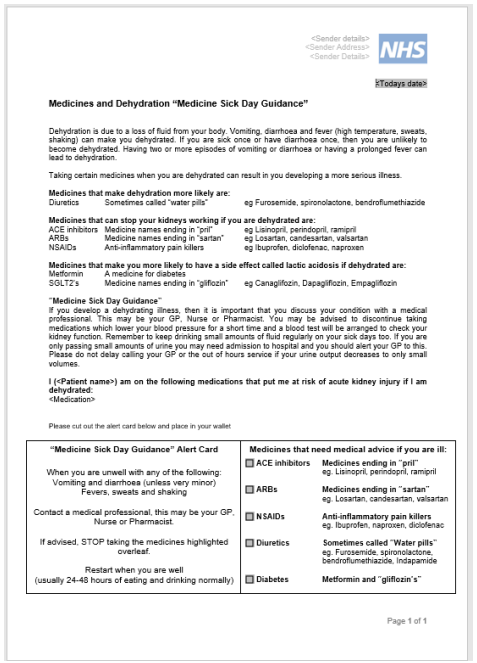
If you become unwell and have vomiting, diarrhoea, or fever, you should stop this medication. You can restart when you are better (eating and drinking normally), however if you remain unwell after 48 hours seek medical advice from your GP, Pharmacist or NHS 111.

The following blood tests are required to monitor your treatment, at least once a year. If you haven't had one in the last year, please book a blood test with your GP practice.

Blood Test	My last results	Reason for test
HbA1c	<Numerics>	To monitor diabetes (if prescribed for diabetes)
eGFR	<Numerics>	To check how your kidneys are working
Creatinine	<Numerics>	To check how your kidneys are working

Notes:

Your next appointment is:



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<Todays date>

Medicines and Dehydration "Medicine Sick Day Guidance"

Dehydration is due to a loss of fluid from your body. Vomiting, diarrhoea and fever (high temperature, sweats, shaking) can make you dehydrated. If you are sick once or have diarrhoea once, then you are unlikely to become dehydrated. Having two or more episodes of vomiting or diarrhoea or having a prolonged fever can lead to dehydration.

Taking certain medicines when you are dehydrated can result in you developing a more serious illness.

Medicines that make dehydration more likely are:
Diuretics — Sometimes called "water pills" — eg Furosemide, spironolactone, bendroflumethiazide

Medicines that can stop your kidneys working if you are dehydrated are:
ACE inhibitors — Medicine names ending in "pril" — eg Lisinopril, perindopril, ramipril
ARBs — Medicine names ending in "sartan" — eg Losartan, candesartan, valsartan
NSAIDs — Anti-inflammatory pain killers — eg Ibuprofen, diclofenac, naproxen

Medicines that make you more likely to have a side effect called lactic acidosis if dehydrated are:
Metformin — A medicine for diabetes
SGLT2's — Medicine names ending in "gliflozin" — eg Canagliflozin, Dapagliflozin, Empagliflozin

"Medicine Sick Day Guidance"
If you develop a dehydrating illness, then it is important that you discuss your condition with a medical professional. This may be your GP, Nurse or Pharmacist. You may be advised to discontinue taking medications which lower your blood pressure for a short time and a blood test will be arranged to check your kidney function. Remember to keep drinking small amounts of fluid regularly on your sick days too. If you are only passing small amounts of urine you may need admission to hospital and you should alert your GP to this. Please do not delay calling your GP or the out of hours service if your urine output decreases to only small volumes.

I (<Patient name>) am on the following medications that put me at risk of acute kidney injury if I am dehydrated:
<Medication>

Please cut out the alert card below and place in your wallet

"Medicine Sick Day Guidance" Alert Card	Medicines that need medical advice if you are ill:	
When you are unwell with any of the following: Vomiting and diarrhoea (unless very minor) Fevers, sweats and shaking Contact a medical professional, this may be your GP, Nurse or Pharmacist. If advised, STOP taking the medicines highlighted overleaf. Restart when you are well (usually 24-48 hours of eating and drinking normally)	☐ ACE inhibitors	Medicines ending in "pril" eg. Lisinopril, perindopril, ramipril
	☐ ARBs	Medicines ending in "sartan" eg. Losartan, candesartan, valsartan
	☐ NSAIDs	Anti-inflammatory pain killers eg. Ibuprofen, naproxen, diclofenac
	☐ Diuretics	Sometimes called "Water pills" eg. Furosemide, spironolactone, bendroflumethiazide, Indapamide
	☐ Diabetes	Metformin and "gliflozin's"

SGLT2 Inhibitors

To swop or to add?

Existing Regime:

Adjusting medication when adding Dapagliflozin for cardiorenal protection (oral only)			
Current regime includes:	Suggested adjustment following discussion with patient:	Monitoring needed:	
		HbA1c target met:	HbA1c target not met:
Metformin only	Up titrate to maximum tolerated dose of Metformin and add Dapagliflozin.	Repeat HbA1c as per normal schedule (6-12months).	Repeat HbA1c after 3 months and escalate treatment if target still not met.
Gliclazide (or other Sulfonylurea)	Add Dapagliflozin and reduce dose of Sulfonylurea by 50%	Check fasting blood glucose levels for 1 week after changes. Gliclazide can be reduced or stopped as appropriate.	Repeat HbA1c after 3 months and escalate treatment if target still not met.
Alogliptin/Linagliptin Saxagliptin/Sitagliptin	Swap for Dapagliflozin.	Repeat HbA1c as per normal schedule (6-12months).	Repeat HbA1c after 3 months and escalate treatment if target still not met.
Pioglitazone	Add Dapagliflozin if HbA1c above target.	n/a	Repeat HbA1c after 3 months and escalate treatment if target still not met.

SGLT2 Inhibitors

To stop or continue?

NICE (NG28) advises that if a person achieves HbA1c below target should encourage to maintain unless hypoglycaemia.

Very low risk of SGLT2i causing hypoglycaemia (unless in combination with a sulfonylurea or insulin).

When eGFR<45 glycaemic effect minimal but still cardio and renal protective.

Discuss with Specialist when eGFR drops to ESKD (eGFR <15)

Diabetes and Frailty

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Diabetes and Frailty

Aim to reduce over treatment of blood glucose

Consider renal function, hypoglycaemic risk, HbA1c and individualise treatment targets for individual patients

Table 3: Recommended therapeutic targets and treatment de-escalation thresholds[9]

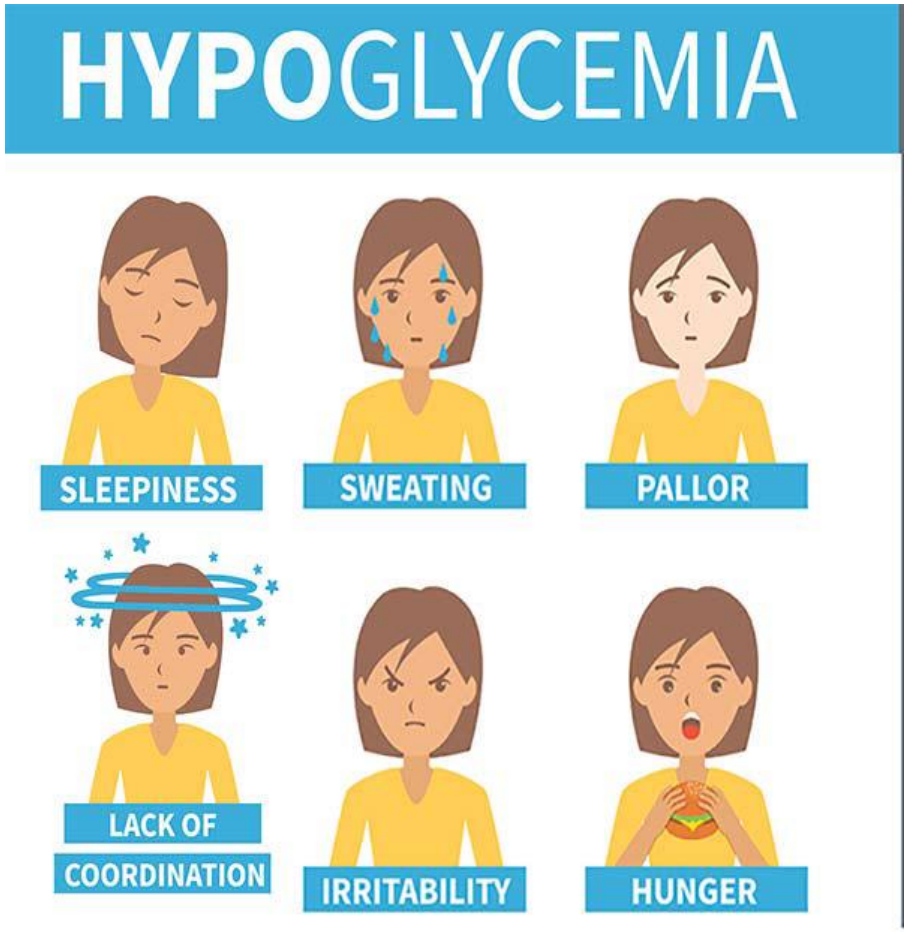
	De-escalation threshold		Treatment target	
	Threshold	**Suggested interventions**	**Targets**	**Interventions**
The fit older adult with diabetes	53 mmol/mol (7.0%)	Evaluate long-acting sulfonylurea and insulin therapy that may cause hypoglycaemia. Consider appropriate dosage in setting of renal function.	58 mmol/mol (7.5%)	Avoid initiating new agents that may cause hypoglycaemia or exaggerate weight loss.
Moderate–severe frailty	58 mmol/mol (7.5%)	Discontinue any sulfonylurea if HbA_{1c} below threshold. Avoid TZDs because of risk of heart failure. Cautious use of insulin and metformin mindful of renal function.	64 mmol/mol (8.0%)	DPP-4 inhibitors and longer-acting insulins have demonstrated safety. TZDs may increase risk of heart failure. SGLT-2 inhibitors may provide additional benefit in people with heart failure but also exacerbate symptoms of diabetes.
Very severe frailty	64 mmol/mol (8.0%)	Withdraw sulfonylureas and short-acting insulins because of risk of hypoglycaemia. Review timings and suitability of NPH insulin with regard to risk of hypoglycaemia. Therapies that promote weight loss may exacerbate sarcopenia.	70 mmol/mol (8.5%)	DPP-4 inhibitors at renally appropriate dose for those close to target. Consider once-daily morning NPH insulin or analogue alternatives if symptomatic nocturnal hyperglycaemia. Educate carers and relatives regarding risk of hypoglycaemia.

HbA_{1c} =glycated haemoglobin; TZD=thiazolidinediones; DPP-4=dipeptidyl peptidase-4; SGLT-2=sodium-glucose co-transporter-2; NPH=neutral protamine Hagedorn

Strain W, Hope S, Green A, Kar P, Valabhji J, Sinclair A. Type 2 diabetes mellitus in older people: a brief statement of key principles of modern day management including the assessment of frailty. A national collaborative stakeholder initiative. *Diabet Med* 2018; **35** (7): 838–845.

Recognising Hypoglycaemia

Where level of glucose in the blood is too low (<4) Can affect everyone differently.



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Insulin Formulary

Formulary website to be updated shortly

Approved May 22

High Strength Rapid Acting Insulin	
Consider using a high strength rapid acting insulin where severe insulin resistance and requirement to use more than 20 units of rapid acting insulin per day.	
Humalog® *(insulin lispro 200 units/mL)*	*KwikPen®* £58.92

Ultra Rapid Acting Insulin	
Consider if post prandial hyperglycaemia.	
Fiasp® *(insulin aspart 100 units/mL)*	*FlexTouch®* pen £30.60
Lyumjev® *(insulin lispro100 units/mL)*	Vial £16.61 Cartridge £28.31 KwikPen £29.46
***Lyumjev® 200units/mL* also available. Please ensure the correct product is selected when prescribing.**	

Type 2 Diabetes	
NPH (neutral protamine Hagedorn) Insulin	
Injected once or twice daily according to need. [NICE 2022]	
Insuman® Basal *(isophane insulin 100 units/mL)*	Cartridge £17.50 Solostar® pen £19.80
Humulin® I *(isophane insulin 100 units/mL)*	Vial £15.68 Cartridge £19.08 KwikPen® £21.70

Short Acting Insulin
Consider starting both NPH and short acting insulin (particularly if HbA1c > 75), administered either separately or as a pre-mixed (biphasic) human insulin preparation. [NICE 2022]

Biosimilar Insulins

> ***Always prescribe insulin by brand!***

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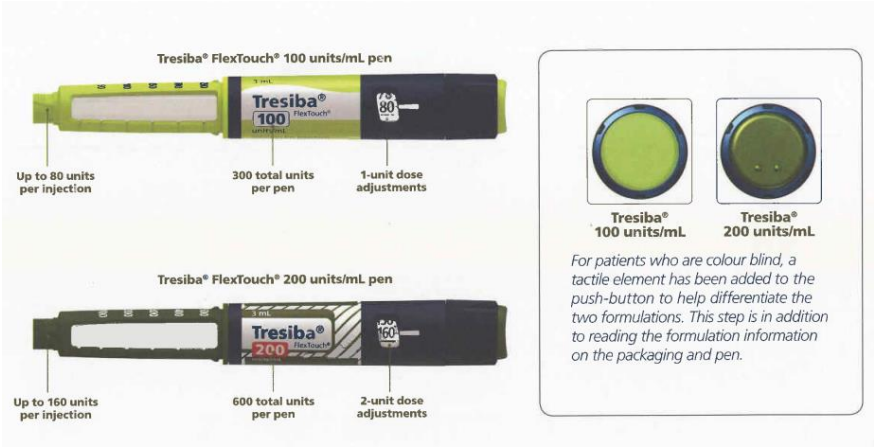
High Strength Insulins



Care when prescribing

[The Six steps to insulin safety]

Prescribing Information

Wiltshire CCG Medicines Management (Medicines - Medicines (bswpartnership.nhs.uk))

Formulary (bswformulary.nhs.uk)

Quarterly Practice Reports (CCG)

Newsletters – BSW Medicines Optimisation Update “MOP-UP”

Eclipse – Diabetes dashboard (Swindon only)

SystmOne

Arden’s templates

Clinical Reporting –Prescribing alerts; diabetes

Specialist Team	Telephone	Email
BaNES DSN	07876 265064	ruh-tr.bathdsnsupport@nhs.net
Swindon DSN	01793 463841	SWICCG.CommunityDiabetesService@nhs.net
Wiltshire DSN	North, East and West 01248 456 483 South 012722 425 176	whc.diabetesnurses@nhs.net

Updated NICE Diabetes Guidance for Glucose Monitoring

“On Thursday 31st March 2022, the National Institute for Health and Care Excellence (NICE) updated the recommendations in their Diabetes guidance in relation to glucose monitoring.

BSW CCG are aware of this updated guidance and people with diabetes should be assured that we are working closely with local Diabetes Specialist colleagues and other local stakeholders in relation to the implementation of this updated guidance, with the aim to maximise benefits, prioritise people with Diabetes with the greatest clinical need, and allow all people with diabetes access to the best possible treatment for their clinical circumstances. We would politely ask our people with diabetes to please bear with us whilst we complete this process.

Further information will be released when available in due course.”

The updated guidance relates to continuous glucose monitoring which is usually managed via the local Specialist Diabetes service:

Type 1 diabetes in Adults - https://www.nice.org.uk/guidance/ng17/chapter/Recommendations#continuous-glucose-monitoring

Type 1 and Type 2 diabetes in Children and Young People – https://www.nice.org.uk/guidance/ng18/chapter/Recommendations#continuous-glucose-monitoring

Type 2 Diabetes in Adults - https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#continuous-glucose-monitoring

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Keen to know more?

Community of Practice

To join, email Alison Evans
whc.diabetesprofessionaleducation@nhs.net

BSW Training Hub Calender link

Eden Complement Plus Link

An award winning 6 month diabetes digital learning programme for Clinical Pharmacists. It aims to increase knowledge and confidence, and enhance the skill levels in caring for people living with diabetes.

An Integrated Career and Competency Framework for Pharmacists in Diabetes Link